```
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* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  FEB 28  PATDPAFULL - New display fields provide for legal status
                  data from INPADOC
 NEWS  4  FEB 28  BABS - Current-awareness alerts (SDIs) available
 NEWS  5  MAR 02  GBFULL: New full-text patent database on STN
 NEWS  6  MAR 03  REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  7  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  8  MAR 22  KOREAPAT now updated monthly; patent information enhanced
 NEWS  9  MAR 22  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  10 MAR 22  PATDPASPC - New patent database available
 NEWS  11 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  12 APR 04  EPFULL enhanced with additional patent information and new
                  fields
 NEWS  13 APR 04  EMBASE - Database reloaded and enhanced
 NEWS  14 APR 18  New CAS Information Use Policies available online
 NEWS  15 APR 25  Patent searching, including current-awareness alerts (SDIs),
                  based on application date in CA/CAplus and USPATFULL/USPAT2
                  may be affected by a change in filing date for U.S.
                  applications.
 NEWS  16 APR 28  Improved searching of U.S. Patent Classifications for
                  U.S. patent records in CA/CAplus
 NEWS  17 MAY 23  GBFULL enhanced with patent drawing images
 NEWS  18 MAY 23  REGISTRY has been enhanced with source information from
                  CHEMCATS
 NEWS  19 JUN 06  The Analysis Edition of STN Express with Discover!
                  (Version 8.0 for Windows) now available
 NEWS  20 JUN 13  RUSSIAPAT: New full-text patent database on STN
 NEWS  21 JUN 13  FRFULL enhanced with patent drawing images
 NEWS  22 JUN 27  MARPAT displays enhanced with expanded G-group definitions
                  and text labels
 NEWS  23 JUL 01  MEDICONF removed from STN
 NEWS  24 JUL 07  STN Patent Forums to be held in July 2005
 NEWS  25 JUL 13  SCISEARCH reloaded
 NEWS  26 JUL 20  Powerful new interactive analysis and visualization software,
                  STN AnaVist, now available
 NEWS  27 AUG 11  Derwent World Patents Index(R) web-based training during
                  August
 NEWS  28 AUG 11  STN AnaVist workshops to be held in North America

 NEWS EXPRESS  JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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FILE 'HOME' ENTERED AT 11:15:52 ON 29 AUG 2005

=> FILE REG
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    0.42       0.42

FILE 'REGISTRY' ENTERED AT 11:16:56 ON 29 AUG 2005
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DICTIONARY FILE UPDATES:  28 AUG 2005  HIGHEST RN 861926-07-0

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*************************************************************
*                                                           *
* The CA roles and document type information have been removed from *
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* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                           *
*************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available.  For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> ....Testing the current file.... screen

ENTER SCREEN EXPRESSION OR (END):end


=>
Uploading C:\Program Files\Stnexp\Queries\DEHYDROPHENYLAHISTINS.str
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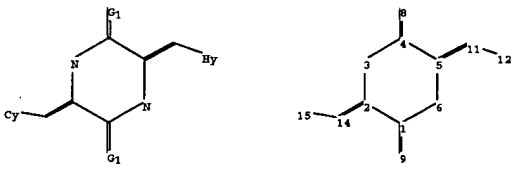


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chain nodes :
8  9  11  12  14  15
ring nodes :
1  2  3  4  5  6
chain bonds :
1-9  2-14  4-8  5-11  11-12  14-15
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-2  1-6  1-9  2-3  3-4  4-5  4-8  5-6  11-12  14-15
exact bonds :
2-14  5-11
isolated ring systems :
containing 1 :


G1:O,S,N

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  8:CLASS  9:CLASS  11:CLASS  12:Atom
 14:CLASS  15:Atom
Generic attributes :
12:
Saturation            : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System    : Monocyclic
15:
Number of Carbon Atoms : less than 7
Type of Ring System    : Monocyclic



L1      STRUCTURE UPLOADED

=> que L1

L2   QUE L1

=> D L2
L2 HAS NO ANSWERS
L1              STR
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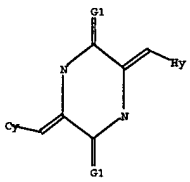


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G1 O,S,N


Structure attributes must be viewed using STN Express query preparation.
L2              QUE  ABB=ON  PLU=ON  L1


=> S L2
SAMPLE SEARCH INITIATED 11:18:22 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    189 TO ITERATE

100.0% PROCESSED      189 ITERATIONS                          16 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          2956 TO     4604
PROJECTED ANSWERS:               80 TO      560

L3            16 SEA SSS SAM L1

=> FILE CAPLUS
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                    1.29       1.71

FILE 'CAPLUS' ENTERED AT 11:18:35 ON 29 AUG 2005
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FILE COVERS 1907 - 29 Aug 2005  VOL 143 ISS 10
FILE LAST UPDATED: 28 Aug 2005  (20050828/ED)

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```

```
=> S L3
L4            0 L3

=> FILE REG
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.45       2.16

FILE 'REGISTRY' ENTERED AT 11:18:54 ON 29 AUG 2005
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**********************************************************************
*                                                                    *
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* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> S L3 SSS FULL
FULL SEARCH INITIATED 11:19:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   3965 TO ITERATE

100.0% PROCESSED     3965 ITERATIONS                          348 ANSWERS
SEARCH TIME: 00.00.04

L5          348 SEA SSS FUL L1

=> FILE CAPLUS
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               161.33     163.49

FILE 'CAPLUS' ENTERED AT 11:19:09 ON 29 AUG 2005
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FILE COVERS 1907 - 29 Aug 2005  VOL 143 ISS 10
FILE LAST UPDATED: 28 Aug 2005  (20050828/ED)

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=> S L5
L6           39 L5

=> D L4 1-8

L4   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:531299  CAPLUS
DN   141:89370
TI   Preparation of dehydrophenylahistins and analogs for treating cancer and
     fungal infection
IN   Hayashi, Yoshio; Grodberg, Jennifer; Palladino, Michael
PA   Nereus Pharmaceuticals, Inc., USA
SO   PCT Int. Appl., 148 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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PI   WO 2004054498       A2     20040701    WO 2003-US24232          20030801
     WO 2004054498       A3     20041125
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
            PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
            TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2494049          AA     20040701    CA 2003-2494049          20030801
     US 2005090667       A1     20050428    US 2003-632531           20030801
     EP 1529044          A2     20050511    EP 2003-811651           20030801
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-401074P     P      20020802
     US 2002-411128P     P      20020916
     US 2003-450063P     P      20030224
     WO 2003-US24232     W      20030801
OS   MARPAT 141:89370

L4   ANSWER 2 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2002:585058  CAPLUS
DN   138:231267
TI   Novel Inhibitors of Plasminogen Activator Inhibitor-1: Development of New
     Templates From Diketopiperazines
AU   Wang, Shouming; Golec, Julian; Miller, Warren; Milutinovic, Sandra;
     Folkes, Adrian; Williams, Susannah; Brooks, Teresa; Hardman, Kevin;
     Charlton, Peter; Wren, Stephen; Spencer, John
CS   Department of Medicinal Chemistry, Xenova Ltd., Slough, Berkshire, SL1
     4NL, UK
SO   Bioorganic & Medicinal Chemistry Letters (2002), 12(17), 2367-2370
     CODEN: BMCLE8; ISSN: 0960-894X
PB   Elsevier Science Ltd.
DT   Journal
LA   English
OS   CASREACT 138:231267
RE.CNT  33     THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 3 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2001:674625  CAPLUS
DN   136:85797
TI   Synthesis and in vitro evaluation of a series of diketopiperazine
     inhibitors of plasminogen activator inhibitor-1
AU   Folkes, A.; Roe, M. B.; Sohal, S.; Golec, J.; Faint, R.; Brooks, T.;
     Charlton, P.
CS   Xenova Limited, Slough, Berks, SL1 4NL, UK
SO   Bioorganic & Medicinal Chemistry Letters (2001), 11(19), 2589-2592
     CODEN: BMCLE8; ISSN: 0960-894X
PB   Elsevier Science Ltd.
DT   Journal
LA   English
OS   CASREACT 136:85797
RE.CNT  24     THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4   ANSWER 4 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1996:188887  CAPLUS
DN   124:261069
TI   Preparation of 3-(phenyl, 2-thienyl, and 2-furanyl)methylene-2,5-
     dioxopiperazine derivatives as inhibitors of plasminogen activator
     inhibitor
IN   Bryans, Justin Stephen; Folkes, Adrian John; Latham, Christopher John
PA   Xenova Ltd., UK
SO   PCT Int. Appl., 74 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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PI   WO 9532190          A2     19951130    WO 1995-GB1180           19950524
     WO 9532190          A3     19951214
         W:  AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI,
             GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD,
             MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ,
             TM, TT
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
     CA 2190279          AA     19951130    CA 1995-2190279          19950524
     AU 9525334          A1     19951218    AU 1995-25334            19950524
     AU 688048           B2     19980305
     ZA 9504226          A      19960122    ZA 1995-4226             19950524
     GB 2303851          A1     19970305    GB 1996-24251            19950524
     GB 2303851          B2     19980506
     EP 760812           A1     19970312    EP 1995-919549           19950524
         R:  DE, ES, FR, GB, IT, NL
     JP 10500425         T2     19980113    JP 1995-530151           19950524
     US 5750530          A      19980512    US 1996-750020           19961217
PRAI GB 1994-10387       A      19940524
     WO 1995-GB1180      W      19950524
OS   MARPAT 124:261069

L4   ANSWER 5 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1995:994199  CAPLUS
DN   124:55981
TI   Preparation of 3,6-bis(benzylidene)piperazine-2,5-diones as multidrug
     resistance modulators
IN   Bryans, Justin Stephen; Latham, Christopher John; Brocchini, Stephen James
PA   Xenova Ltd., UK
SO   PCT Int. Appl., 70 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
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PI   WO 9521830          A1     19950817    WO 1995-GB300            19950214
         W:  AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI,
             GB, GE, HU, JP, KE, KG, KP, MD, MG, MN, MW, MX, NL, NO, NZ, PL,
             PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG, US, UZ, VN
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
     GB 2286394          A1     19950816    GB 1995-2872             19950214
     GB 2286394          B2     19980812
     AU 9515884          A1     19950829    AU 1995-15884            19950214
     ZA 9501181          A      19960814    ZA 1995-1181             19950214
     US 5852018          A      19981222    US 1996-693171           19961104
PRAI GB 1994-2809        A      19940214
     WO 1995-GB300       W      19950214
OS   MARPAT 124:55981

L4   ANSWER 6 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   1995:994198  CAPLUS
DN   124:55980
TI   Preparation of piperazinedione-derivative multiple drug resistance
     modulators
IN   Brocchini, Stephen James; Bryans, Justin Stephen; Latham, Christopher
     John; Folkes, Adrian John
PA   Xenova Ltd., UK
SO   PCT Int. Appl., 70 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
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PI   WO 9521831          A1     19950817    WO 1995-GB301            19950214
         W:  AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI,
             GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG,
             MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT,
             UA, US
         RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT,
             LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE,
             SN, TD, TG
     GB 2286392          A1     19950816    GB 1995-2860             19950214
     GB 2286392          B2     19980812
     AU 9516676          A1     19950829    AU 1995-16676            19950214
     ZA 9501175          A      19960814    ZA 1995-1175             19950214
     US 5861400          A      19990119    US 1996-693169           19961104
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PRAI GB 1994-2805 A 19940214
WO 1995-GB301 W 19950214
OS MARPAT 124:55980

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:994197 CAPLUS
DN 124:55979
TI Preparation of piperazinedione-derivative inhibitors of plasminogen activator inhibitor
IN Brocchini, Stephen James; Bryans, Justin Stephen; Folkes, Adrian John; Latham, Christopher John; Brumwell, Julie Elizabeth
PA Xenova Ltd., UK
SO PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9521832	A1	19950817	WO 1995-GB302	19950214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
GB 2286395	A1	19950816	GB 1995-2874	19950214
GB 2286395	B2	19980826		
CA 2182877	AA	19950817	CA 1995-2182877	19950214
AU 9516677	A1	19950829	AU 1995-16677	19950214
AU 693159	B2	19980625		
ZA 9501180	A	19960814	ZA 1995-1180	19950214
EP 745070	A1	19961204	EP 1995-908314	19950214
R: DE, ES, FR, GB, IT, NL				
JP 09509157	T2	19970916	JP 1995-521082	19950214
US 5891877	A	19990406	US 1996-693172	19960925
PRAI GB 1994-2807	A	19940214		
WO 1995-GB302	W	19950214		

OS MARPAT 124:55979

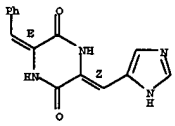
L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1988:630947 CAPLUS
DN 109:230947
TI Conjugated systems derived from piperazine-2,5-dione
AU Katritzky, Alan R.; Fan, Wei Qiang; Szajda, Maria; Li, Qiao Ling; Caster, Kenneth C.
CS Dep. Chem., Univ. Florida, Gainesville, FL, 32611, USA
SO Journal of Heterocyclic Chemistry (1988), 25(2), 591-7
CODEN: JHTCAD; ISSN: 0022-152X
DT Journal
LA English
OS CASREACT 109:230947

ELIMINATES APPLICANTS

=> S L6 NOT 2004:531299/AN
L1 2004:531299/AN
L7 38 L6 NOT 2004:531299/AN

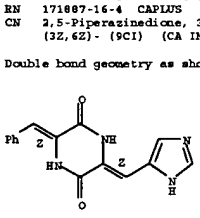
=> D 1-39 IBIB ABS HITSTR

L7 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1066409 CAPLUS
DOCUMENT NUMBER: 143:133671



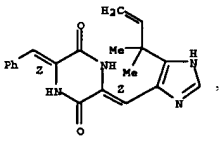
IT **171887-16-4P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(enzymic synthesis of dehydro cyclo(His-Phe)s, analogs of the potent cell cycle inhibitor, dehydrophenylahistin, and their inhibitory activities toward cell division)
RN 171887-16-4 CAPLUS
CN 2,5-Piperazinedione, 3-(1H-imidazol-4-ylmethylene)-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **351325-37-6**, (Z)-Dehydrophenylahistin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(enzymic synthesis of dehydro cyclo(His-Phe)s, analogs of the potent cell cycle inhibitor, dehydrophenylahistin, and their inhibitory activities toward cell division)
RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

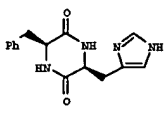
Double bond geometry as shown.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:550739 CAPLUS
DOCUMENT NUMBER: 141:106489

TITLE: Enzymatic synthesis of dehydro cyclo(His-Phe)s, analogs of the potent cell cycle inhibitor, dehydrophenylahistin, and their inhibitory activities toward cell division
AUTHOR(S): Kanzaki, Hiroshi; Yanagisawa, Satohiro; Nitoda, Teruhiko
CORPORATE SOURCE: Laboratory of Bioresources Chemistry, Faculty of Agriculture, Okayama University, Okayama, 700-8530, Japan
SOURCE: Bioscience, Biotechnology, and Biochemistry (2004), 68(11), 2341-2345
CODEN: BBBIEJ; ISSN: 0916-8451
PUBLISHER: Japan Society for Bioscience, Biotechnology, and Agrochemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

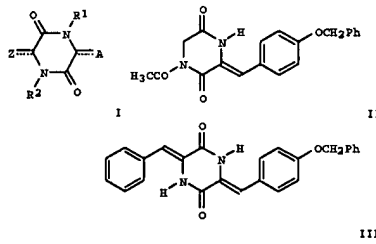
AB Cyclo(His-Phe) (I) was effectively converted to its dehydro derivs. by the enzyme of Streptomyces albulus KO-23, an albonoursin-producing actinomycete. Two types of dehydro derivs. were isolated from the reaction mixture and identified as cyclo(ΔHis-ΔPhe) and cyclo(His-ΔPhe). This is the first report on cyclo-(His- ΔPhe) and the enzymic preparation of both compds. Cyclo(ΔHis-ΔPhe), a tetradehydro cyclic dipeptide, exhibited a min. inhibitory concentration of 0.78 μmol/mL inhibitory activity toward the first cleavage of sea urchin embryos, in contrast to cyclo-(His- ΔPhe) that had no activity. The finding that the isoprenylated derivative of cyclo(ΔHis-ΔPhe), dehydrophyenylahistin, had 2,000 times higher activity than cyclo(ΔHis-ΔPhe) indicates that an isoprenyl group attached to an imidazole ring of the compound was essential for the inhibitory activity.
IT **351325-38-7P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(enzymic synthesis of dehydro cyclo(His-Phe)s, analogs of the potent cell cycle inhibitor, dehydrophenylahistin, and their inhibitory activities toward cell division)
RN 351325-38-7 CAPLUS
CN 2,5-Piperazinedione, 3-(1H-imidazol-4-ylmethylene)-6-(phenylmethylene)-, (3Z,6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

TITLE: Preparation of piperazinediones as antiangiogenic agents.
INVENTOR(S): Teng, Che-ming; Wang, Hui-po; Li, Eric I. C.; Lee, On; Guh, Jih-hwa; Chen, Huei-ting; Fan, Ya-bing; Chen, Ya-lan
PATENT ASSIGNEE(S): Taiwan
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 851,077.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004132738	A1	20040708	US 2003-689865	20031020
US 2002028819	A1	20020307	US 2001-851077	20010508
US 6635649	B2	20031021		
ZA 2002009917	A	20020217	ZA 2002-9917	20021206
PRIORITY APPLN. INFO.:			US 2000-304191P P	20000509
			US 2001-851077 A2	20010508

OTHER SOURCE(S): MARPAT 141:106489
GI

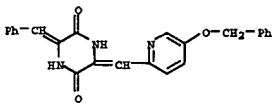


I II III

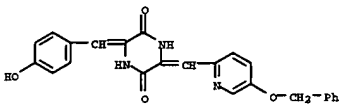
AB Title compds. I [A = H, CHRaRb, CReRb with provisos; Z = CHRcRd, CRcRd with provisos; R1, R2 = H, CORe, COORe; Ra, Rb, Rc, Rd, Re = H, alkyl, aryl, etc.] and their pharmaceutically acceptable salts were prepared For example, condensation of benzaldehyde and piperazinedione II, e.g., prepared from 1,4-diacetylpiperazine-2,5-dione and 5-benzyloxypyridin-2-ylformaldehyde, afforded piperazinedione III as a mixture of isomers. In human umbilical vein endothelial cell (HUVECs) proliferation inhibition assays, a large number of compds. I inhibited HUVECs proliferation. Compds. I of the invention relate to a method for the treatment of angiogenesis related diseases.
IT **380620-78-0P**, 3-[(5-Benzyloxypyridin-2-yl)methylidene]-6-phenylmethylidene piperazine-2,5-dione **380620-80-4P**
380620-82-6P 380620-85-9P 380620-87-1P
380620-89-3P 380620-91-7P 380620-93-9P,
3-[(5-Benzyloxypyridin-2-yl)methylidene]-6-[(thien-2-

yl]methylidene]piperazine-2,5-dione 380620-95-1P, 3-[(5-Benzyloxypyridin-2-yl)methylidene]-6-[(2-pyridinyl)methylidene]piperazine-2,5-dione 380620-97-3P, 3,6-Di[(5-benzyloxypyridin-2-yl)methylidene]piperazine-2,5-dione 380621-13-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazinediones as anti-angiogenic agents.)

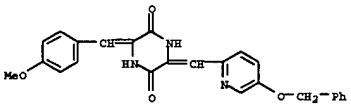
RN 380620-78-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(phenylmethoxy)-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



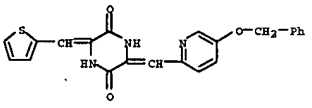
RN 380620-80-4 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-hydroxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



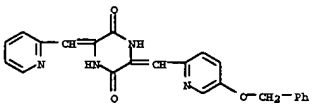
RN 380620-82-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-methoxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



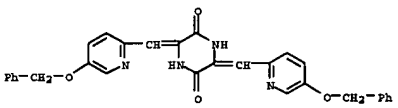
RN 380620-85-9 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-fluorophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



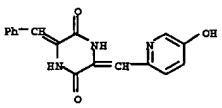
RN 380620-95-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(phenylmethoxy)-2-pyridinyl]methylene]-6-(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)



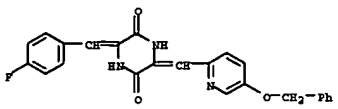
RN 380620-97-3 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis[[5-(phenylmethoxy)-2-pyridinyl]methylene]-(9CI) (CA INDEX NAME)



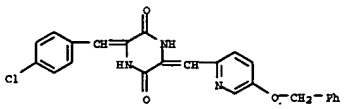
RN 380621-13-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(5-hydroxy-2-pyridinyl)methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



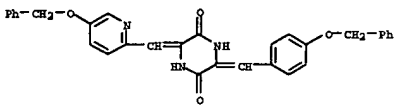
IT 380621-04-5P 380621-05-6P 380621-09-0P 719088-61-6P 719088-71-8P, 3-(5-Benzyloxypyridin-2-ylmethylene)-6-(4-nitrobenzylidene)piperazine-2,5-dione 719088-77-4P, 3-(5-Benzyloxypyridin-2-ylmethylene)-6-(2-nitrobenzylidene)piperazine-2,5-dione 719088-82-1P, 3-(5-Benzyloxypyridin-2-ylmethylene)-6-(3-chlorobenzylidene)piperazine-2,5-dione 719088-87-6P, 3-(5-Benzyloxypyridin-2-ylmethylene)-6-(3,5-dimethoxybenzylidene)-piperazine-2,5-dione 719088-92-3P,



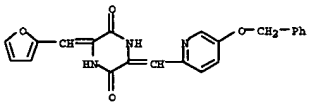
RN 380620-87-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-chlorophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



RN 380620-89-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-(phenylmethoxy)phenyl]methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



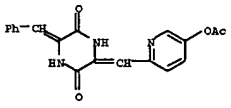
RN 380620-91-7 CAPLUS
CN 2,5-Piperazinedione, 3-(2-furanylmethylene)-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



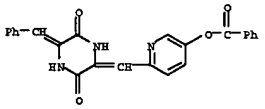
RN 380620-93-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(phenylmethoxy)-2-pyridinyl]methylene]-6-(2-thienylmethylene)- (9CI) (CA INDEX NAME)

3-(5-Benzyloxypyridin-2-ylmethylene)-6-(3,4-dichlorobenzylidene)-piperazine-2,5-dione 719089-02-8P, 3-(5-Benzyloxypyridin-2-ylmethylene)-6-(3-hydroxybenzylidene)piperazine-2,5-dione 719089-10-8P, 3-(5-Benzyloxypyridin-2-ylmethylene)-6-(3,5-dihydroxybenzylidene)-piperazine-2,5-dione
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinediones as anti-angiogenic agents.)

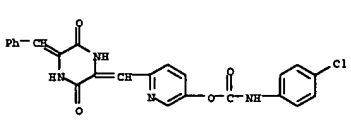
RN 380621-04-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(acetyloxy)-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



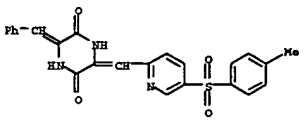
RN 380621-05-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(benzoyloxy)-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



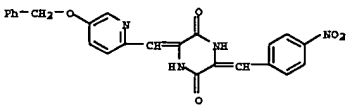
RN 380621-09-0 CAPLUS
CN Carbamic acid, (4-chlorophenyl)-, 6-[[3,6-dioxo-5-(phenylmethylene)piperazinylidene]methyl]-3-pyridinyl ester (9CI) (CA INDEX NAME)



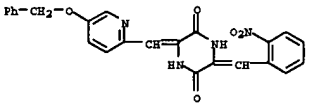
RN 719088-61-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[(4-methylphenyl)sulfonyl]-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



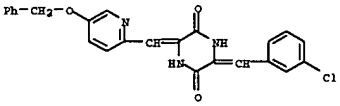
RN 719088-71-8 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-nitrophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



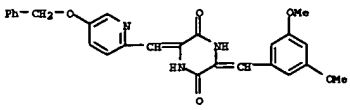
RN 719088-77-4 CAPLUS
CN 2,5-Piperazinedione, 3-[(2-nitrophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



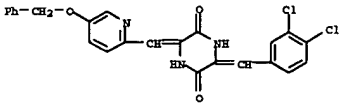
RN 719088-82-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(3-chlorophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



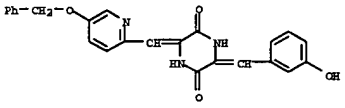
RN 719088-87-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,5-dimethoxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



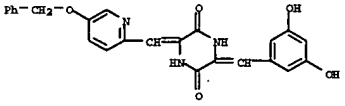
RN 719088-92-3 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,4-dichlorophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



RN 719089-02-8 CAPLUS
CN 2,5-Piperazinedione, 3-[(3-hydroxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



RN 719089-10-8 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,5-dihydroxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)

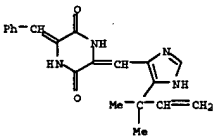


L7 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:406614 CAPLUS
DOCUMENT NUMBER: 141:218132
TITLE: Structure-activity relationship analysis
AUTHOR(S): Hayakawa, Yoichi
CORPORATE SOURCE: Institute of Molecular and Cellular Biosciences, University of Tokyo, Bunkyo-ku, Tokyo, 113-0032, Japan
SOURCE: Gan to Kagaku Ryoho (2004), 31(4), 526-528
CODEN: GTKRDX; ISSN: 0385-0684
PUBLISHER: Gan to Kagaku Ryohosha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review. All samples for anticancer drug screening were classified according to their structural features and their structure-activity relationships were analyzed. Synthetic gymnastatin analogs including JCI: 11788 and JCI: 11786 altered their selectivity for protein kinase inhibition with the length of a fatty acid chain. Although a new inhibitor of tubulin depolymn., JCI: 11578, displayed a high correlation to known tubulin binders, novel inhibitors of tubulin polymerization, JCI: 11534, JCI: 11675 and JCI: 11676, exhibited poor correlations to tubulin binders. JCI: 11403 and JCI: 11407 inhibited topoisomerase I selectively and appear to belong to a new family of topoisomerase inhibitors. They are expected to be important key compds. for structure-activity relation anal. as well as new lead compds. for anticancer drugs.

IT 748804-27-5, JCI 11534
RL: BMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-activity relationship anal. for antitumor agent)

RN 748804-27-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)

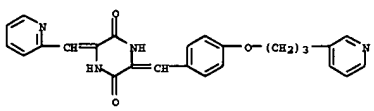


L7 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:302998 CAPLUS
DOCUMENT NUMBER: 140:332040
TITLE: XR5967, a novel modulator of plasminogen activator inhibitor-1 activity, suppresses tumor cell invasion and angiogenesis in vitro
AUTHOR(S): Brooks, Teresa D.; Wang, Shouming W.; Bruenner, Nils; Charlton, Peter A.
CORPORATE SOURCE: Xenova Ltd, Slough, UK
SOURCE: Anti-Cancer Drugs (2004), 15(1), 37-44
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent reports suggest that elevated levels of plasminogen activator inhibitor (PAI)-1 may contribute to tumor progression. We have recently shown that antibodies to PAI-1 block the invasive and migratory potential of human fibrosarcoma cells and suppress angiogenesis in vitro. Here we report the in vitro evaluation of a low-mol.-weight modulator of PAI-1, XR5967, on invasion, migration and angiogenesis. XR5967, a diketopiperazine, dose-dependently inhibited the activity of human and murine PAI-1, towards urokinase plasminogen activator (uPA), with IC50 values of 800 nM and 0.3 μM, resp. This was confirmed by SDS-PAGE, revealing that XR5967 inhibited complex formation between PAI-1 and uPA. This suppression may be caused by XR5967 promoting insertion of the reactive center loop within PAI-1. XR5967 dose-dependently inhibited the invasion of human HT1080 fibrosarcoma cells through Matrigel. Their invasion was reduced by 57% (p<0.001) at 5 μM. HT1080 cell migration was inhibited in a similar manner, indicating that PAI-1 may play an addnl. role in invasion, which is distinct to its role in the regulation of proteolysis. The potential of XR5967 to inhibit the invasion/migration of human endothelial cells was investigated in an in vitro model of angiogenesis. In this model XR5967 reduced tubule formation by 77% at 5 μM (p<0.001), highlighting a crucial role for PAI-1 in angiogenesis. These data stress the importance of a balanced proteolysis in the processes of invasion, migration and angiogenesis. Our results support the clin. findings and indicate that modulation of PAI-1 activity, with low-mol.-weight inhibitor of PAI-1 activity, may be of therapeutic benefit for the treatment of cancer.

IT 680595-26-0
RL: BMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(XR5967, a novel modulator of plasminogen activator inhibitor-1 activity, suppresses tumor cell invasion and angiogenesis in vitro)

RN 680595-26-0 CAPLUS
CN 2,5-Piperazinedione, 3-(2-pyridinylmethylene)-6-[[4-[3-(3-pyridinyl)propoxy]phenyl]methylene]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

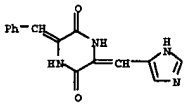
L7 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:1007385 CAPLUS
DOCUMENT NUMBER: 140:54529
TITLE: Streptomyces alb genes for albocoursin biosynthesis and method of preparing diketopiperazine derivatives with transgenic bacteria
INVENTOR(S): Gondry, Muriel; Genet, Roger; Lautru, Sylvie; Pernodet, Jean Luc
PATENT ASSIGNEE(S): Commissariat a l'Energie Atomique, Fr.; Centre National de la Recherche Scientifique CNRS
SOURCE: Fr. Demande, 53 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2841260	A1	20031226	FR 2002-7728	20020621
FR 2841260	B1	20041022		

CA 2490517 AA 20031231 CA 2003-2490517 20030618
WO 2004000879 A1 20031231 WO 2003-FR1851 20030618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, ER, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1523498 A1 20050420 EP 2003-760733 20030618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: FR 2002-7728 A 20020621
WO 2003-FR1851 W 20030618

AB The sequences of S. noursei genes albA, albB, albC, and albD involved in albonoursin biosynthesis as well as the encoded protein sequences are disclosed. These genes may be expressed in other bacteria to produce these proteins. Alternatively, the transgenic bacteria may be used to convert amino acids to diketopiperazine derivs. Thus, S. lividans expressing the albA-C genes (AlbD seems to be involved in dikeotpiperazine transport) converted Phe and Leu to albonoursin, and Trp to the analogous diketopiperazine derivative

IT **637744-26-4P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(streptomyces alb genes for albonoursin biosynthesis and method of preparing dikeotpiperazine derivs. with transgenic bacteria)
RN 637744-26-4 CAPLUS
CN 2,5-Piperazinedione, 3-(1H-imidazol-4-ylmethylene)-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



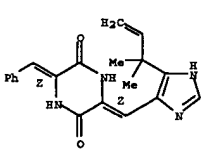
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:698509 CAPLUS
DOCUMENT NUMBER: 140:40915
TITLE: Effective production of potent cell cycle inhibitor dehydrophenylahistin by a combination of chemical racemization and Streptomyces enzyme-catalyzed conversion
AUTHOR(S): Kanzaki, Hiroshi; Ikeda, Banri; Nitoda, Teruhiko
CORPORATE SOURCE: Laboratory of Bioresources Chemistry, Faculty of Agriculture, Okayama University, Okayama, 700-8530, Japan
SOURCE: Actinomycetologica (2003), 17(1), 1-5
CODEN: ACTIF4; ISSN: 0914-5818
PUBLISHER: Society for Actinomycetes Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A review. Cyclic dipeptides (CDPs, diketopiperazines) and their derivs. are widely distributed in nature as secondary metabolites. Although some of dehydro-CDPs are known as cell cycle inhibitors, their effective syntheses have not been reported. The authors found that Streptomyces albulus KO23, an albonoursin-producing actinomycete, had a biosynthetic pathway from cyclo (Leu-Phe) to albonoursin, cyclo (ΔLeu-ΔPhe) by the fed-batch culture and the resting-cell expts. And this enzyme activity was found to be effectively extracted in the cell-free extract of this actinomycete. This is the first report for the dehydrogenation of amino acid residues at α, β-positions in CDPs. Furthermore, this enzyme system enables us to synthesize several didehydro- and tetradehydro-CDPs from the corresponding CDPs. Among dehydro-CDPs prepared, the tetradehydro-CDPs exhibited cytotoxicity, while the didehydro-CDPs had no activity, indicating that dehydrogenation at α, β-positions of both amino acid residues in CDPs is required for cytotoxicity. Based on the above results, we speculated that a tetradehydro-CDP prepared from a didehydro-CDP exhibiting cytotoxicity might be a potent cytotoxic compound Dehydrophenylahistin synthesized by this enzyme system from (-)-phenylahistin, which was recently reported to be a new cell cycle inhibitor, exhibited 1000 times higher inhibitory activity toward the first cleavage of sea urchin embryo than (-)-phenylahistin, and thus, would be a promising lead compound for antitumor agents.

IT **351325-37-6P**, (Z)-Dehydrophenylahistin
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
((Z)-Dehydrophenylahistin; production of bioactive compds. by biosynthetic enzymes of dehydro cyclic dipeptides)
RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



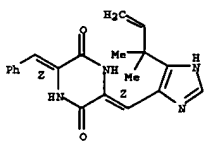
L7 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:339083 CAPLUS
DOCUMENT NUMBER: 139:145715
TITLE: Mapping of the epitope of a monoclonal antibody protecting plasminogen activator inhibitor-1 against inactivating agents

OTHER SOURCE(S): CASREACT 140:40915

AB An effective method was established for preparing the potent cell cycle inhibitor dehydrophenylahistin by a combination of chemical racemization of partially purified (z)-phenylahistin and enzymic conversion of (-)-phenylahistin by the cell-free extract of Streptomyces albulus KO-23, an albonoursin-producing actinomycete. This method enables conversion of (+)-phenylahistin, which is present in the culture of Aspergillus ustus NSC-F038 and is not transformed by the Streptomyces enzyme, to dehydrophenylahistin.

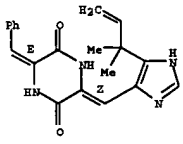
IT **351325-37-6P**
RL: BMP (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(production of dehydrophenylahistin by a combination of chemical racemization
and Streptomyces enzyme-catalyzed dehydrogenation)
RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **507485-39-4P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(production of dehydrophenylahistin by a combination of chemical racemization
and Streptomyces enzyme-catalyzed dehydrogenation)
RN 507485-39-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

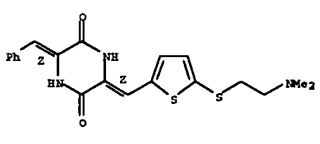
L7 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:612948 CAPLUS
DOCUMENT NUMBER: 140:198105
TITLE: Production of bioactive compounds by biosynthetic

AUTHOR(S): Bodker, Julie S.; Wind, Troels; Jensen, Jan K.; Hansen, Martin; Pedersen, Katrine E.; Andreasen, Peter A.
CORPORATE SOURCE: Laboratory of Cellular Protein Science, Department of Molecular Biology, University of Aarhus, Aarhus, 8000 C, Den.
SOURCE: European Journal of Biochemistry (2003), 270(8), 1672-1679
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasminogen activator inhibitor-1 (PAI-1) belongs to the serpin family of serine proteinase inhibitors. Serpins inhibit their target proteinases by an ester bond being formed between the active site serine of the proteinase and the P1 residue of the reactive center loop (RCL) of the serpin, followed by insertion of the RCL into β-sheet A of the serpin. Concomitantly, there are conformational changes in the flexible joint region lateral to β-sheet A. We have now, by site-directed mutagenesis, mapped the epitope for a monoclonal antibody, which protects the inhibitory activity of PAI-1 against inactivation by a variety of agents acting on β-sheet A and the flexible joint region. Curiously, the epitope is localized in α-helix C and the loop connecting α-helix I and β-strand 5A, on the side of PAI-1 opposite to β-sheet A and distantly from the flexible joint region. By a combination of site-directed mutagenesis and antibody protection against an inactivating organo-chemical ligand, we were able to identify a residue involved in conferring the antibody-induced conformational change from the epitope to the rest of the mol. We have thus provided evidence for communication between secondary structural elements not previously known to interact in serpins.

IT **174766-49-5**, XR5118
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(XR5118, Mab-1 protection of PAI-1 against; mapping of epitope of monoclonal antibody protecting plasminogen activator inhibitor-1 against inactivating agents)
RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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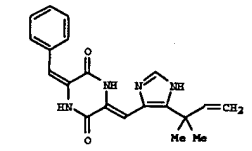
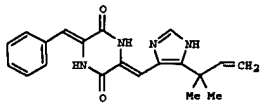
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:11190 CAPLUS
DOCUMENT NUMBER: 138:300224

TITLE: A novel potent cell cycle inhibitor dehydrophenylahistin: Enzymatic synthesis and inhibitory activity toward sea urchin embryo
AUTHOR(S): Kanzaki, Hiroshi; Yanagisawa, Satohiro; Kanoh, Kaneo; Nitoda, Teruhiko
CORPORATE SOURCE: Laboratory of Bioresources Chemistry, Faculty of Agricultre, Okayama University, Okayama, 700-8530, Japan
SOURCE: Journal of Antibiotics (2002), 55(12), 1042-1047
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



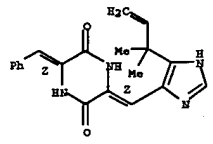
I



II

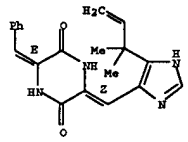
AB A novel dehydrogenated cyclic dipeptide named as dehydrophenylahistin (APLH) (I, II) was effectively prepared from a fungal metabolite (±)-phenylahistin by an enzymic conversion catalyzed by a cell-free extract of Streptomyces albulus KO-23, an albonoursin-producing actinomycete. APLH exhibited > 1000 times as high inhibitory activity toward the first cleavage of sea urchin embryos as phenylahistin, which has been reported to be a cell cycle inhibitor, and > 10,000 as high as albonoursin, indicating that APLH is a promising anticancer drugs.
IT **351325-37-6P, (Z)-Dehydrophenylahistin 507485-39-4P, (E)-Dehydrophenylahistin**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of novel cell cycle inhibitor dehydrophenylahistin from fungal metabolite)
RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 507485-39-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6E)- (9CI) (CA INDEX NAME)

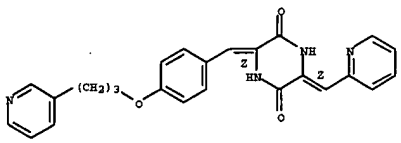
Double bond geometry as shown.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

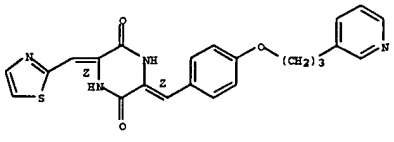
L7 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:585058 CAPLUS
DOCUMENT NUMBER: 138:231267
TITLE: Novel Inhibitors of Plasminogen Activator Inhibitor-1: Development of New Templates From Diketopiperazines
AUTHOR(S): Wang, Shouming; Golec, Julian; Miller, Warren; Milutinovic, Sandra; Folkes, Adrian; Williams, Susannah; Brooks, Teresa; Hardman, Kevin; Charlton, Peter; Wren, Stephen; Spencer, John
CORPORATE SOURCE: Department of Medicinal Chemistry, Xenova Ltd., Slough, Berkshire, SL1 4NL, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(17), 2367-2370
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:231267
AB Several isoquinoline-based templates were identified from the studies of the conformational effects of the diketopiperazine structures for PAI-1 inhibition. Moderate to good activity was retained with the elimination of unattractive characteristics in the diketopiperazine template.
IT **501942-29-6P 501942-31-0P 501942-33-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure-activity relationship of diketopiperazines as novel inhibitors of plasminogen activator inhibitor-1)
RN 501942-29-6 CAPLUS
CN 2,5-Piperazinedione, 3-(2-pyridinylmethylene)-6-[[4-[3-(3-pyridinyl)propoxy]phenyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



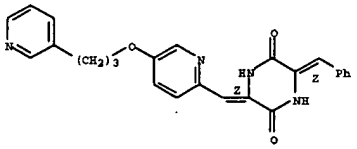
RN 501942-31-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(3-pyridinyl)propoxy]phenyl]methylene]-6-(2-thiazolylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 501942-33-2 CAPLUS
CN 2,5-Piperazinedione, 3-(phenylmethylene)-6-[[5-[3-(3-pyridinyl)propoxy]-2-pyridinyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

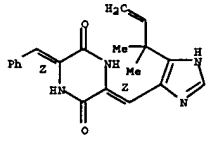
Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:581841 CAPLUS
DOCUMENT NUMBER: 137:277822
TITLE: Production of novel bioactive compounds by cyclic dipeptide dehydrogenase
AUTHOR(S): Kanzaki, Hiroshi
CORPORATE SOURCE: Grad. Sch. of Nat. Sci. & Technol., Okayama Univ., Okayama, 700-8530, Japan
SOURCE: Baiosaiensu to Indasutori (2002), 60(7), 454-457
CODEN: BIDSE6; ISSN: 0914-8981
PUBLISHER: Baioindasutori Kyokai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on enzymic preparation of a novel bioactive compound dehydrophenylahistin with strong cell division-inhibiting activity by dehydrogenation of phenylahistin, a secondary metabolite derived from Aspergillus ustus, using albonoursin biosynthesis enzymes from Streptomyces albulus. Possible application of dehydrophenylahistin to tumor chemotherapy is also discussed.
IT **351325-37-6P**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); BIOL (Biological study); PREP (Preparation)
(production of novel bioactive compound dehydrophenylahistin with cell division-inhibiting activity by cyclic dipeptide dehydrogenase)
RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



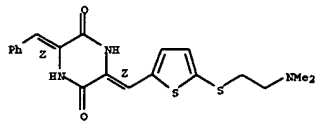
L7 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:576581 CAPLUS
DOCUMENT NUMBER: 138:147428
TITLE: Characterization and comparative evaluation of a novel PAI-1 inhibitor
AUTHOR(S): Gils, Ann; Stassen, Jean-Marie; Nar, Herbert; Kley, Joerg T.; Wienen, Wolfgang; Ries, Uwe J.; Declerck, Paul J.
CORPORATE SOURCE: Laboratory for Pharmaceutical Biology and Phytopharmacology, Faculty of Pharmaceutical Sciences, Katholieke Universiteit Leuven, Louvain, B-3000, Belg.
SOURCE: Thrombosis and Haemostasis (2002), 88(1), 137-143
CODEN: THHADQ; ISSN: 0340-6245
PUBLISHER: Schattauer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plasminogen activator inhibitor-1 (PAI-1), the primary physiol. inhibitor of both tissue-type plasminogen activator and urokinase-type plasminogen activator in plasma, is a well established risk factor in thrombotic diseases. Reduction of active PAI-1 levels may lead to a decreased tendency of thrombosis. Compds. that can suppress pharmacol. active PAI-1 levels are therefore considered as putative drugs. In the present study, we describe the PAI-1 neutralising properties and mechanism of a newly selected compound (i.e. fendosal, HP129) in comparison to four previously reported ccmpds. (i.e. AR-H029953XX, XR1853, XR5118 and the peptide TVASS) using different assays. The inhibitory effect of these compds. on active PAI-1 was analyzed by a plasmin-coupled chromogenic assay (Coaset t-PA), direct chromogenic assays (t-PA, u-PA) and quantification of complex formation by ELISA, SDS-PAGE and surface plasmon resonance. Comparative

evaluation of the obtained IC50 values reveals large differences (i.e. IC50 of 15 μM (HP129) vs. >1000 μM (XR5118) determined at 37° using SDS-PAGE) between the compds. studied. Importantly, the relative potency of the various compds. is also dependent on the method used (10 to 170-fold differences in IC50 values). Characterization of the PAI-1 forms (i.e. active, non-reactive and substrate) generated upon inactivation reveals that the newly described compound HP129 induces a unique pathway (i.e. active to non-reactive conversion via substrate-behaving intermediate) of inactivation compared to the other compds. Taken together, these data strongly suggest that the various compds. act through different mechanisms. In addition, the results stress the necessity for a careful selection of the method used for the evaluation of PAI-1 inhibitors, preferably requiring a panel of screening methods.

IT **174766-49-5, XR5118**
RL: BMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization and comparative evaluation of a novel PAI-1 inhibitor)

RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-([2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HCl

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

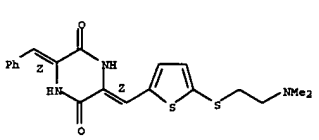
L7 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:525518 CAPLUS
DOCUMENT NUMBER: 137:277821
TITLE: Chemical information-guided enzymatic synthesis of bioactive compounds
AUTHOR(S): Kanzaki, Hiroshi
CORPORATE SOURCE: Grad. Sch. Nat. Sci., Okayama Univ., Japan
SOURCE: Nippon Nogei Kagaku Kaishi (2002), 76(6), 539-541
CODEN: NNKKAA; ISSN: 0002-1407
PUBLISHER: Nippon Nogei Kagakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on chemical information-guided enzymic synthesis of dehydro cyclic dipeptides with cytotoxic activity, discussing databases and information systems in natural science, dehydro cyclic dipeptide albonoursin biosynthesis system in Streptomyces albulus KO23, bioconversion of cyclic dipeptides to dehydro derivs. using albonoursin biosynthesis system and their cell division-inhibiting activity, and preparation of dehydrophenylahistin with higher cell division-inhibiting activity.

IT **351325-37-6P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(chemical information-guided enzymic synthesis of bioactive compds., focusing on preparation of dehydro cyclic dipeptides with cytotoxic activity)

RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● HCl

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:923566 CAPLUS
DOCUMENT NUMBER: 136:37627
TITLE: Preparation of piperazinediones as antitumor agents
INVENTOR(S): Teng, Che-Ming; Wang, Hui-Pong; Li, Eric I. C.; Lee, On; Ouh, Jih-Hwa; Chen, Huei-Ting; Fan, Ya-Bing; Chen, Ya-Lan
PATENT ASSIGNEE(S): Adpharma, Inc., Taiwan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095858	A2	20011220	WO 2001-US14721	20010508
WO 2001095858	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2408649	AA	20011220	CA 2001-2408649	20010508
AU 2001094505	A5	20011224	AU 2001-94505	20010508
EP 1282609	A2	20030212	EP 2001-975152	20010508
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001010745	A	20031230	BR 2001-10745	20010508
JP 2004510701	T2	20040408	JP 2002-510040	20010508
NO 2002005373	A	20021213	NO 2002-5373	20021108
ZA 2002009917	A	20020217	ZA 2002-9917	20021206
PRIORITY APPLN. INFO.:			US 2000-304191P	P 20000509
			US 2000-567271	A1 20000509
			WO 2001-US14721	W 20010508

OTHER SOURCE(S): MARPAT 136:37627
GI

(CA INDEX NAME)

Double bond geometry as shown.

● HCl

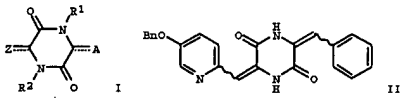
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:416179 CAPLUS
DOCUMENT NUMBER: 137:212721
TITLE: The role of β-strand 5A of plasminogen activator inhibitor-1 in regulation of its latency transition and inhibitory activity by vitronectin
AUTHOR(S): Jensen, Signe; Kirkegaard, Tove; Pedersen, Katrine E.; Busse, Marta; Preissner, Klaus T.; Rodenburg, Kees W.; Andreasen, Peter A.
CORPORATE SOURCE: Department of Molecular and Structural Biology, Laboratory of Cellular Protein Science, Aarhus University, Aarhus, DK-8000 C, Den.
SOURCE: Biochimica et Biophysica Acta (2002), 1597(2), 301-310
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasminogen activator inhibitor-1 (PAI-1) is a potential target for anti-thrombotic and anti-cancer therapy. It circulates in plasma in a complex with vitronectin (VN). We have studied biochem. mechanisms for PAI-1 neutralization and its modulation by VN, using site-directed mutagenesis and limited proteolysis. We demonstrate that VN, besides delaying conversion of PAI-1 to the inactive latent form, also protects PAI-1 against cold- and detergent-induced substrate behavior and counteracts conversion of PAI-1 to inert forms by certain amphipathic organochem. compds. VN protection against cold- and detergent-induced substrate behavior is associated with inhibition of the proteolytic susceptibility of β-strand 5A. Alanine substitution of a lysine residue placed centrally in β-strand 5A implied a VN-induced acceleration of latency transition, instead of the normal delay. This substitution not only protects PAI-1 against neutralization, but also counteracts VN-induced protection against neutralization. We conclude that β-strand 5A plays a crucial role in VN-regulation of PAI-1 activity.

IT **174766-49-5, XR5118**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vitronectin counteracts conversion of plasminogen activator inhibitor-1 to inert forms by organochem. compds.)

RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI)

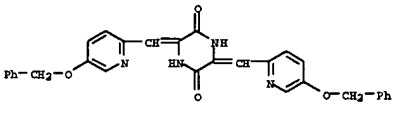


I II

AB The title compds. [I; A = H, CHRaRb or CRaRb; Z = R3OArB (wherein B = CHRc or CRc; Ar = heteroaryl; R3 = H, alkyl, aryl, etc.); R1, R2 = H, COR4, CO2R4, CONR4R5, or SO2R4; Ra-Re = H, alkyl, aryl, etc.], useful in treating cancer, were prepared Thus, reacting 1,4-diacetylpiperazine-2,5-dione with 5-benzyloxypyridin-2-ylformaldehyde in the presence of Et3N in DMF followed by reaction of the resulting 1-acetyl-3-[(5-benzyloxypyridin-2-yl)methylidine]piperazine-2,5-dione with PhCHO in the presence of Et3N in DMF afforded the title compound II. Compds. I were tested against a panel of 60 different NCI human tumor cell lines. The most potent compound I exhibited GI50 of <10-4 M for all 60 cell lines, with GI50 of <10-8 M for 9 cell lines.

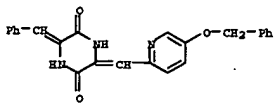
IT **380620-97-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazinediones as antitumor agents)

RN 380620-97-3 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)

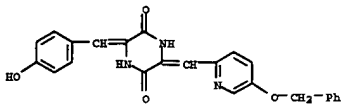


IT **380620-78-0P 380620-80-4P 380620-82-6P**
380620-85-9P 380620-87-1P 380620-89-3P
380620-91-7P 380620-93-9P 380620-95-1P
380621-04-5P 380621-05-6P 380621-07-8P
380621-09-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinediones as antitumor agents)

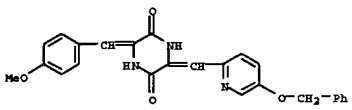
RN 380620-78-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(phenylmethoxy)-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



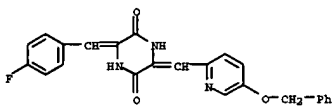
RN 380620-80-4 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-hydroxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



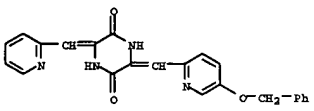
RN 380620-82-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-methoxyphenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



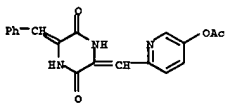
RN 380620-85-9 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-fluorophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



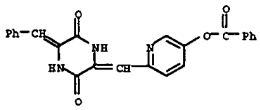
RN 380620-87-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-chlorophenyl)methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



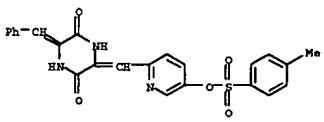
RN 380621-04-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(acetyloxy)-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



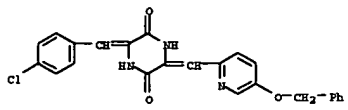
RN 380621-05-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(benzoyloxy)-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



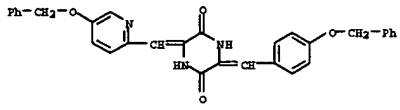
RN 380621-07-8 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[(4-methylphenyl)sulfonyl]oxy]-2-pyridinyl]methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



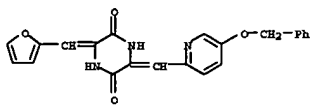
RN 380621-09-0 CAPLUS
CN Carbamic acid, (4-chlorophenyl)-, 6-[[3,6-dioxo-5-(phenylmethylene)piperazinylidene]methyl]-3-pyridinyl ester (9CI) (CA INDEX NAME)



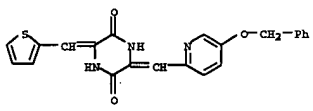
RN 380620-89-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-(phenylmethoxy)phenyl]methylene]-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



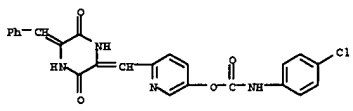
RN 380620-91-7 CAPLUS
CN 2,5-Piperazinedione, 3-(2-furanylmethylene)-6-[[5-(phenylmethoxy)-2-pyridinyl]methylene]- (9CI) (CA INDEX NAME)



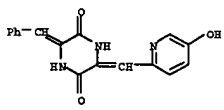
RN 380620-93-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(phenylmethoxy)-2-pyridinyl]methylene]-6-(2-thienylmethylene)- (9CI) (CA INDEX NAME)



RN 380620-95-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(phenylmethoxy)-2-pyridinyl]methylene]-6-(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)

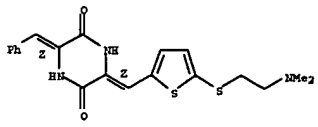


IT **380621-13-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinediones as antitumor agents)
RN 380621-13-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(5-hydroxy-2-pyridinyl)methylene]-6-(phenylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:674625 CAPLUS
DOCUMENT NUMBER: 136:85797
TITLE: Synthesis and in vitro evaluation of a series of diketopiperazine inhibitors of plasminogen activator inhibitor-1
AUTHOR(S): Folkes, A.; Roe, M. B.; Sohal, S.; Golec, J.; Faint, R.; Brooks, T.; Charlton, P.
CORPORATE SOURCE: Xenova Limited, Slough, Berks, SL1 4NL, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(19), 2589-2592
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:85797
AB A series of diketopiperazine-based inhibitors of PAI-1 was synthesized and evaluated. These studies resulted in the identification of 9-[4-[[5-[[4-[(2-thienyl)carbonylamino]phenyl]methylene]-3,6-dioxo-2-piperazinylidene]methyl]phenoxy]octanoic acid which inhibited PAI-1 in vitro with an IC50=0.2 μM. The synthesis and SAR of these compds. are described.
IT **174766-49-5C**, XR 5110, bis-arylidenediketopiperazine derivative
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation and evaluation of diketopiperazines as inhibitors of plasminogen activator inhibitor-1)
RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

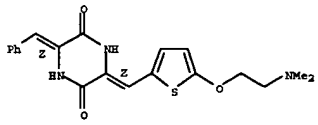


● HCl

IT 171887-61-9P 174766-35-9P 174766-36-0P
174766-37-1P 174766-41-7P 174849-93-5P
174849-95-7P 174849-96-8P 174849-98-0P
174850-04-5P 386212-63-1P 386212-64-2P
386212-65-3P
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and evaluation of diketopiperazines as inhibitors of plasminogen activator inhibitor-1)

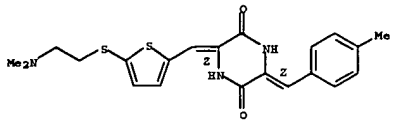
RN 171887-61-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[2-(dimethylamino)ethoxy]-2-thienyl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

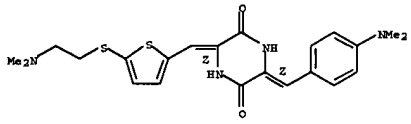


RN 174766-35-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-methylphenyl)methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

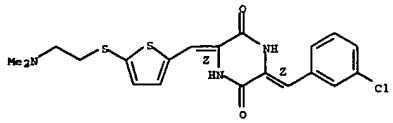


RN 174766-36-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-methoxyphenyl)methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)



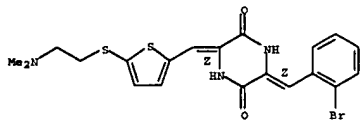
RN 174849-95-7 CAPLUS
CN 2,5-Piperazinedione, 3-[(3-chlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174849-96-8 CAPLUS
CN 2,5-Piperazinedione, 3-[(2-bromophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

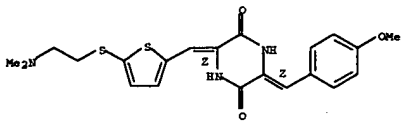
Double bond geometry as shown.



RN 174849-98-0 CAPLUS
CN Benzonitrile, 4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]- (9CI) (CA INDEX NAME)

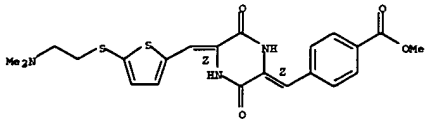
Double bond geometry as shown.

Double bond geometry as shown.



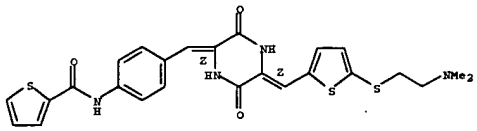
RN 174766-37-1 CAPLUS
CN Benzoic acid, 4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



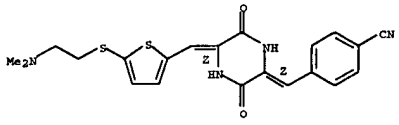
RN 174766-41-7 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]phenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



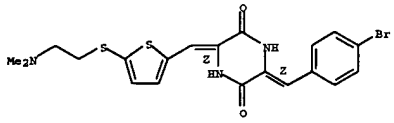
RN 174849-93-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(dimethylamino)phenyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



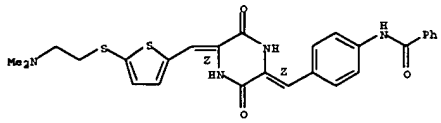
RN 174850-04-5 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-bromophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



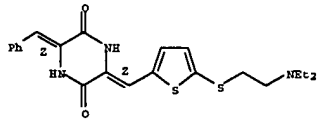
RN 386212-63-1 CAPLUS
CN Benzamide, N-[4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]phenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



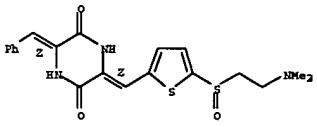
RN 386212-64-2 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(diethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 386212-65-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]sulfinyl]-2-thienyl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



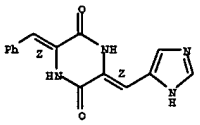
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:545688 CAPLUS
DOCUMENT NUMBER: 135:127218
TITLE: Cell division inhibitors and process for producing the same
INVENTOR(S): Kanzakik, Hiroshi; Kanoh, Kaneo; Yangisawa, Satohiro; Nitoda, Teruhiko; Akazawa, Kazumi
PATENT ASSIGNEE(S): Nippon Steel Corp., Japan; Nippon Steel Chemical Co., Ltd
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053290	A1	20010726	WO 2000-JP6807	20000929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2403790	AA	20010726	CA 2000-2403790	20000929
AU 2000074511	A5	20010731	AU 2000-74511	20000929
BR 2000017067	A	20021022	BR 2000-17067	20000929
EP 1264831	A1	20021211	EP 2000-963011	20000929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
NZ 519989	A	20040528	NZ 2000-519989	20000929
ZA 2002006576	A	20030512	ZA 2002-6576	20020816
PRIORITY APPLN. INFO.:			JP 2000-9370 A	20000118
			WO 2000-JP6807 W	20000929

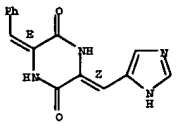
OTHER SOURCE(S): MARPAT 135:127218
AB Disclosed are cell division inhibitors containing as the active ingredient various dehydrodiketopiperazines such as dehydrophenylahistin or analogs thereof and dehydrogenases and a process for producing the same.
IT 171887-16-4P 351325-38-7P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dehydrogenation of cyclophenylalanylhistidyl using Streptomyces albulus enzyme)
RN 171887-16-4 CAPLUS
CN 2,5-Piperazinedione, 3-(1H-imidazol-4-ylmethylene)-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



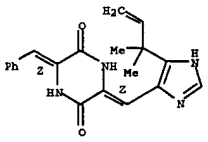
RN 351325-38-7 CAPLUS
CN 2,5-Piperazinedione, 3-(1H-imidazol-4-ylmethylene)-6-(phenylmethylene)-, (3Z,6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 351325-37-6P
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dehydrogenation of phenylahistin using Streptomyces albulus enzyme)
RN 351325-37-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-(1,1-dimethyl-2-propenyl)-1H-imidazol-4-yl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

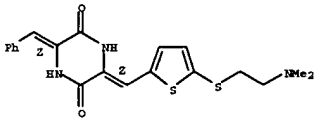
Double bond geometry as shown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:318521 CAPLUS
DOCUMENT NUMBER: 135:104178
TITLE: A regulatory hydrophobic area in the flexible joint region of plasminogen activator inhibitor-1, defined with fluorescent activity-neutralizing ligands. Ligand-induced serpin polymerization
AUTHOR(S): Egelund, Rikke; Einholm, Anja P.; Pedersen, Katrine E.; Nielsen, Rasmus W.; Christensen, Anni; Deinum, Johanna; Andreasen, Peter A.
CORPORATE SOURCE: Laboratory of Cellular Protein Science, Department of Molecular and Structural Biology, Aarhus University, Aarhus, 8000, Den.
SOURCE: Journal of Biological Chemistry (2001), 276(16), 13077-13086
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have characterized the neutralization of the inhibitory activity of the serpin plasminogen activator inhibitor-1 (PAI-1) by a number of structurally distinct organo-chems., including compds. with environment-sensitive spectroscopic properties. In contrast to latent and reactive center-cleaved PAI-1 and PAI-1 in complex with urokinase-type plasminogen activator (uPA), active PAI-1 strongly increased the fluorescence of the PAI-1-neutralizing compds. 1-anilinonaphthalene-8-sulfonic acid and 4,4'-dianilino-1,1'-binaphthyl-5,5'-disulfonic acid. The fluorescence increase could be competed by all tested non-fluorescent neutralizers, indicating that all neutralizers bind to a common hydrophobic area preferentially accessible in active PAI-1. Activity neutralization proceeded through two consecutive steps as follows: first step is conversion to forms displaying substrate behavior toward uPA, and second step is to forms inert to uPA. With some neutralizers, the second step was associated with PAI-1 polymerization Vitronectin reduced the susceptibility to the neutralizers. Changes in sensitivity to activity neutralization by point mutations were compatible with the various neutralizers having overlapping, but not identical, binding sites in the region around α-helixes D and E and β-strand 1A, known to act as a flexible joint when β-sheet A opens and the reactive center loop inserts as β-strand 4A during reaction with target proteinases. The defined binding area may be a target for development of compds. for neutralizing PAI-1 in cancer and cardiovascular diseases.
IT 174766-49-5, YR5118
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neutralizing ligand; identification of a regulatory hydrophobic area in the flexible joint region of plasminogen activator inhibitor-1, defined with fluorescent activity-neutralizing ligands and ligand-induced serpin polymerization)
RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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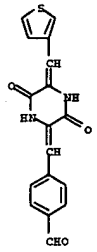
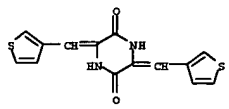
REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

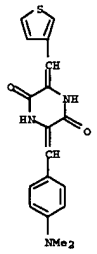
L7 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:433951 CAPLUS
DOCUMENT NUMBER: 134:56642
TITLE: New conjugated systems derived from piperazine-2,5-dione
AUTHOR(S): Asiri, Abdullah Mohamed
CORPORATE SOURCE: Chemistry Department, Faculty of Science, King Abdul-Aziz University, Jeddah, 21413, Saudi Arabia
SOURCE: Molecules [Electronic Publication] (2000), 5(3), 629-636
CODEN: MOLEFW; ISSN: 1420-3049
URL: http://www.mdpi.org/molecules/papers/50300629.pdf
PUBLISHER: Molecular Diversity Preservation International
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:56642
AB The preparation of monoarylidene and both sym. and unsym. bisarylidene derivs. of piperazine-2,5-dione is described. The use of 1,4-diacetylpiperazine-2,5-dione makes it possible to prepare unsym. bisarylidenes. The introduction of a dicyanomethylene moiety into the para position of one of the arylidene groups gave a remarkable deepening in the color of the resulting compds.
IT 313951-85-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of mono- and bisarylidenepiperazinediones)
RN 313951-85-8 CAPLUS
CN Benzaldehyde, 4-[[3,6-dioxo-5-(3-thienylmethylene)piperazinylidene]methyl]- (9CI) (CA INDEX NAME)



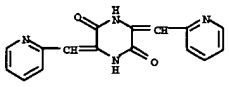
IT **313951-81-4P 313951-84-7P 313951-86-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of mono- and bisarylidenepiperazinediones)
RN 313951-81-4 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(3-thienylmethylene)- (9CI) (CA INDEX NAME)



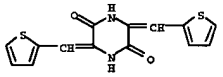
RN 313951-84-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-(dimethylamino)phenyl]methylene]-6-(3-thienylmethylene)- (9CI) (CA INDEX NAME)



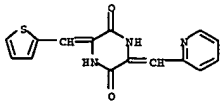
RN 313951-86-9 CAPLUS



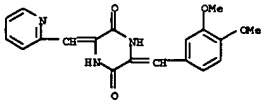
RN 105975-15-3 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-thienylmethylene)- (9CI) (CA INDEX NAME)



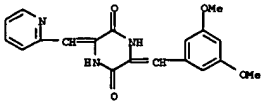
RN 261952-63-0 CAPLUS
CN 2,5-Piperazinedione, 3-(2-pyridinylmethylene)-6-(2-thienylmethylene)- (9CI) (CA INDEX NAME)



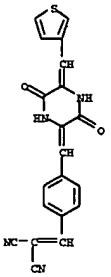
RN 261952-64-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,4-dimethoxyphenyl)methylene]-6-(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)



RN 261952-65-2 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,5-dimethoxyphenyl)methylene]-6-(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)



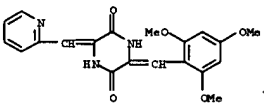
CN Propanedinitrile, [[4-[[3,6-dioxo-5-(3-thienylmethylene)piperazinylidene]methyl]phenyl]methylene]- (9CI) (CA INDEX NAME)



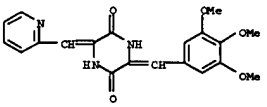
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:93997 CAPLUS
DOCUMENT NUMBER: 132:237061
TITLE: Solution-phase combinatorial synthesis and evaluation of piperazine-2,5-dione derivatives
AUTHOR(S): Loughlin, Wendy A.; Marshall, Raymond L.; Carreiro, Adelina; Elson, Kathryn E.
CORPORATE SOURCE: School of Science, Griffith University, Brisbane, 4111, Australia
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(2), 91-94
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:237061
AB An efficient one-pot synthesis of a 61-membered combinatorial chemical library of piperazine-2,5-diones was accomplished. Results of combinatorial synthesis, purification, anal., and biol. evaluation are described.
IT **7670-69-1P 105975-15-3P 261952-63-0P**
261952-64-1P 261952-65-2P 261952-66-3P
261952-67-4P 261952-68-5P 261952-69-6P
261952-70-9P 261952-71-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solution-phase combinatorial synthesis and cytotoxicity of piperazinediones)
RN 7670-69-1 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)

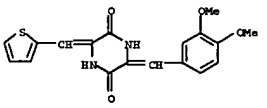
RN 261952-66-3 CAPLUS
CN 2,5-Piperazinedione, 3-(2-pyridinylmethylene)-6-[(2,4,6-trimethoxyphenyl)methylene]- (9CI) (CA INDEX NAME)



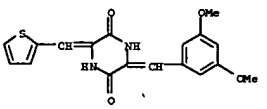
RN 261952-67-4 CAPLUS
CN 2,5-Piperazinedione, 3-(2-pyridinylmethylene)-6-[(3,4,5-trimethoxyphenyl)methylene]- (9CI) (CA INDEX NAME)



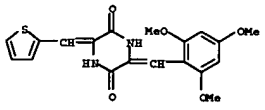
RN 261952-68-5 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,4-dimethoxyphenyl)methylene]-6-(2-thienylmethylene)- (9CI) (CA INDEX NAME)



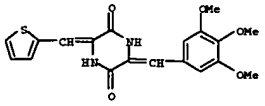
RN 261952-69-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,5-dimethoxyphenyl)methylene]-6-(2-thienylmethylene)- (9CI) (CA INDEX NAME)



RN 261952-70-9 CAPLUS
CN 2,5-Piperazinedione, 3-(2-thienylmethylene)-6-[(2,4,6-trimethoxyphenyl)methylene]- (9CI) (CA INDEX NAME)



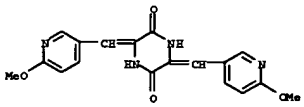
RN 261952-71-0 CAPLUS
CN 2,5-Piperazinedione, 3-(2-thienylmethylene)-6-[(3,4,5-trimethoxyphenyl)methylene]- (9CI) (CA INDEX NAME)



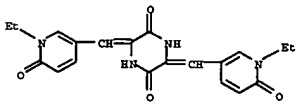
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:268698 CAPLUS
DOCUMENT NUMBER: 131:99171
TITLE: Transition-State Stabilization by a Mammalian Reductive Dehalogenase
AUTHOR(S): Kunishima, Munetaka; Friedman, Jessica E.; Rokita, Steven E.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, University of Maryland, College Park, MD, 20742, USA
SOURCE: Journal of the American Chemical Society (1999), 121(19), 4722-4723
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:99171
AB Mammals have the ability to promote reductive deiodination of the hormone thyroxine (3-[4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]alanine), its metabolites, and related intermediates including iodotyrosine. A series of selenoenzymes found in tissues such as brown fat, liver, kidney, and the central nervous system are responsible for the reduction and deiodination of thyroxine and the concomitant oxidation of glutathione. In contrast, an iodide salvage enzyme in the thyroid mediates reduction and deiodination of iodo- and diiodotyrosine with consumption of NADPH. Little mechanistic data has yet to be gathered on these mammalian reactions and we now report compelling evidence for a key intermediate proposed in catalysis of iodotyrosine deiodinase. A series of pyridinyl amino acids were prepared and shown to be reversible and competitive inhibitors of substrate diiodotyrosine turnover under standard assay conditions.
IT 230648-38-1P 230648-44-9P 230648-46-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(transition-state stabilization by iodotyrosine deiodinase)

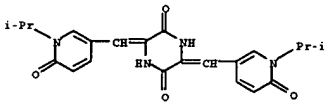
RN 230648-38-1 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis[(6-methoxy-3-pyridinyl)methylene]- (9CI) (CA INDEX NAME)



RN 230648-44-9 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis[(1-ethyl-1,6-dihydro-6-oxo-3-pyridinyl)methylene]- (9CI) (CA INDEX NAME)



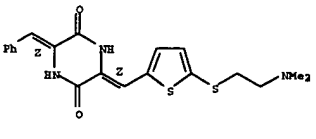
RN 230648-46-1 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis[(1,6-dihydro-1-(1-methylethyl)-6-oxo-3-pyridinyl)methylene]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:563777 CAPLUS
DOCUMENT NUMBER: 127:214885
TITLE: Novel low-molecular-weight inhibitor of PAI-1 (XR5118) promotes endogenous fibrinolysis and reduces postthrombolysis thrombus growth in rabbits
AUTHOR(S): Friederich, Philip W.; Levi, Marcel; Biemond, Bart J.; Charlton, Peter; Templeton, David; Van Zonneveld, Anton Jan; Bevan, Paul; Pannekoek, Hans; Ten Cate, Jan W.
CORPORATE SOURCE: Center for Hemostasis, Thrombosis, Atherosclerosis, Inflammation Research, Academic Medical Center, University of Amsterdam, Amsterdam, 1105 AZ, Neth.
SOURCE: Circulation (1997), 96(3), 916-921
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Elevated levels of plasminogen activator inhibitor 1 (PAI-1) have been associated with the occurrence of thrombotic disease, and inhibition of PAI-1 activity in vivo resulted in enhanced thrombolysis and a reduction in reocclusion. Besides monoclonal antibodies and peptides, no suitable agents that are able to block PAI-1 activity are available to date. The present study was designed to test the interaction between a nonantibody, nonpeptide, diketopiperazine-based inhibitor of PAI-1, XR5118, and PAI-1 and to assess the effect of XR5118 on PAI-1 activity in vitro and on in vivo thrombolysis and thrombus growth in an exptl. thrombosis model in rabbits. The binding site of XR5118 on the PAI-1 mol. was studied by competitive binding expts. with mapped anti-PAI-1 monoclonal antibodies by use of surface plasmon resonance expts. XR5118 selectively and competitively inhibited binding of the PAI-1-inhibiting monoclonal antibody CLB-2C9, indicating that binding of XR5118 to PAI-1 takes place at the area between amino acids 110 and 145 of the PAI-1 mol., which is known to be involved with the binding of PAI-1 to tissue plasminogen activator (TPA). Incubation of plasma or platelet release with XR5118 resulted in a dose-dependent inhibition of PAI-1 activity. Systemic infusion of XR5118 induced a significant reduction in plasma PAI-1 activity levels from 23.7 to 10.9 IU/mL. Administration of XR5118 resulted in a significant, twofold increase in endogenous thrombolysis compared with the control. Thrombus growth in rabbits receiving both XR5118 and rTPA was significantly attenuated compared with rabbits receiving rTPA alone (13.5% vs. 19.9%, resp.). XR5118 binds to PAI-1 and reduces plasma PAI-1 activity levels. Furthermore, XR5118 promotes endogenous thrombolysis and inhibits thrombus accretion and is the first nonpeptide compound with significant anti-PAI-1 activity in vivo in these models.
IT 174766-49-5, XR5118
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(novel low-mol.-weight inhibitor of PAI-1 (XR5118) promotes endogenous fibrinolysis and reduces postthrombolysis thrombus growth in rabbits and its use with recombinant tissue plasminogen activator)
RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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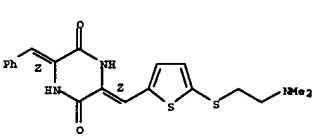
L7 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:272695 CAPLUS
DOCUMENT NUMBER: 127:570
TITLE: XR5118, a novel modulator of plasminogen activator inhibitor-1 (PAI-1), increases endogenous tPA activity in the rat
AUTHOR(S): Charlton, P.; Paint, R.; Barnes, C.; Bent, F.; Folkes, A.; Templeton, D.; Mackie, I.; Machin, S.; Bevan, P.
CORPORATE SOURCE: Xenova Limited, Slough, UK
SOURCE: Fibrinolysis & Proteolysis (1997), 11(1), 51-56
CODEN: FBPRFP
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal
LANGUAGE: English
AB XR5118, a diketopiperazine-based low mol. weight inhibitor of plasminogen activator inhibitor-1 (PAI-1) activity, was studied ex vivo and in vivo in the rat to determine whether inhibition of PAI-1 activity resulted in increased fibrinolysis and protection against thrombus formation. XR5118 reversed the inhibitory effects of human PAI-1 against tissue-type plasminogen activator (tPA), in an vitro amidolytic assay (S2251) with an IC50 value of 3.5 μM±0.19 μM (n=7). This activity was confirmed in in vitro fibrinolysis assays against both human and rat PAI-1 and, following i.v. administration to rats, XR5118 (1-5 mg/kg) dose-dependently increased clot lysis in an ex vivo dilute blood clot lysis time (DBCLT) assay. At 5 mg/kg, XR5118 increased clot lysis by 41±1.6% (n=39, P<0.01) relative to vehicle control. In a rat model of arterial thrombosis, i.v. infusion of XR5118 (0.5 mg/kg/min for 20 min) significantly prolonged the time to thrombus formation from 21.2±2.5 min in the vehicle-treated group to 37.0±5.4 min (n=10 per group, P<0.01). Furthermore, infusion of XR5118 was associated with a significant decrease in plasma PAI-1 activity and a significant increase in plasma tPA activity. Thus, in the rat, XR5118 enhanced fibrinolysis ex vivo, increased endogenous tPA activity, and attenuated arterial thrombus formation following elec. injury. As elevated PAI-1 has been proposed as a risk factor in thrombotic disease, inhibition of PAI-1 activity may have utility in the treatment of thromboembolic disease.
IT 174766-49-5, XR 5118
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increase of endogenous tPA activity in antithrombotic and fibrinolytic mechanism of PAI-1 modulator XR5118)
RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:534871 CAPLUS

DOCUMENT NUMBER: 125:195689
TITLE: Preparation of piperazine-2,5-dione derivatives as multidrug resistance modulators
INVENTOR(S): Ashworth, Philip Anthony; Hunjan, Sukhjit; Pretswell, Ian Andrew; Ryder, Hamish; Brocchini, Stephen James
PATENT ASSIGNEE(S): Xenova Limited, UK
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9620190	A1	19960704	WO 1995-GB3027	19951222
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9510909	A	19960830	ZA 1995-10909	19951221
CA 2207500	AA	19960704	CA 1995-2207500	19951222
AU 9643100	A1	19960719	AU 1996-43100	19951222
AU 698828	B2	19981105		
EP 799222	A1	19971008	EP 1995-941797	19951222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
GB 2311781	A1	19971008	GB 1997-12184	19951222
GB 2311781	B2	19980916		
CN 1175253	A	19980304	CN 1995-197672	19951222
JP 10511384	T2	19981104	JP 1995-520301	19951222
HU 77943	A2	19981228	HU 1998-398	19951222
BR 9510410	A	19990908	BR 1995-10410	19951222
FI 9702660	A	19970822	FI 1997-2660	19970619
NO 9702937	A	19970623	NO 1997-2937	19970623
US 6635454	B1	20031021	US 2000-573629	20000517

PRIORITY APPLN. INFO.:
GB 1994-26224 A 19941223
DE 1994-4447387 A 19941222
WO 1995-GB3027 W 19951222
US 1997-860339 A3 19971125

OTHER SOURCE(S): MARPAT 125:195689
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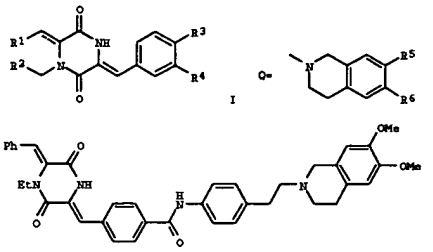


I

II

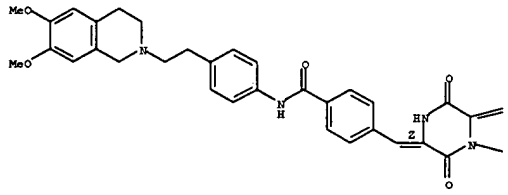
AB Title compds. [I; R1 = (un)substituted Ph, heterocyclyl, (cyclo)alkyl, etc.; R2 = H, alkyl, CO2H, Ph, etc.; 1 of R3,R4 = CONHZ(CH2)qR; R = tetrahydroisoquinolino group Q; R5,R6 = H or alkoxy; R5R6 = OCH2O; Z = bond or 1,4-phenylene; q = 1-4; dashed line = optional bond] were prepared Thus, IC50 for doxorubicin + title compound II against AR 1.0 cell proliferation was 10-3 that for doxorubicin alone.

IT 180598-01-0P 180598-06-5P 180598-07-6P
180598-08-7P 180598-09-8P 180598-12-3P
180598-24-7P 180598-25-8P 180598-26-9P
180598-27-0P 180598-28-1P 180598-29-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazine-2,5-dione derivs. as multidrug resistance modulators)

RN 180598-01-0 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-4-[[5-(3-furanylmethylene)-4-methyl-3,6-dioxopiperazinylidene]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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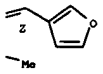
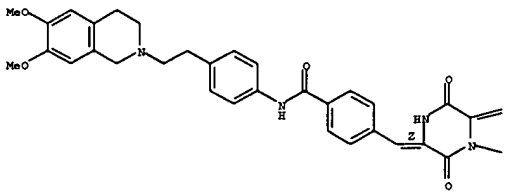
PAGE 1-B



RN 180598-06-5 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-4-[[4-methyl-3,6-dioxo-5-(3-pyridinylmethylene)piperazinylidene]methyl]-, dihydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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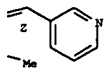
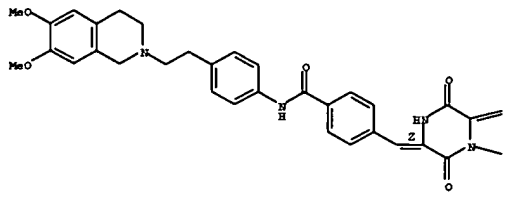
PAGE 1-B



RN 180598-07-6 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-4-[[4-methyl-3,6-dioxo-5-(3-thienylmethylene)piperazinylidene]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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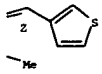
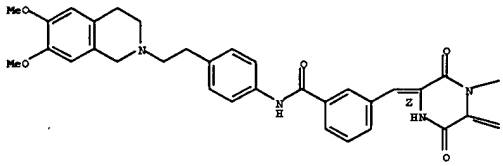
PAGE 1-B



RN 180598-08-7 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-3-[[4-methyl-3,6-dioxo-5-(2-thienylmethylene)piperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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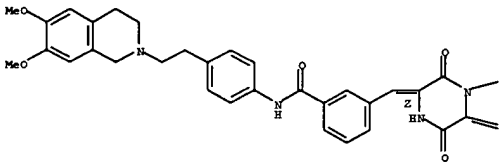

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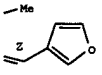
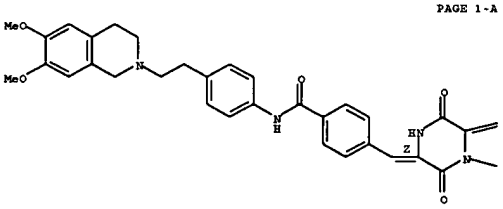


RN 180598-24-7 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-4-[[5-(2-furanylmethylene)-4-methyl-3,6-dioxopiperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

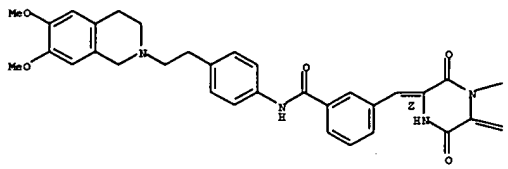


PAGE 1-B

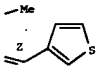
RN 180598-09-8 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-3-[[4-methyl-3,6-dioxo-5-(3-thienylmethylene)piperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



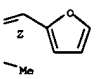
PAGE 1-B



RN 180598-12-3 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-3-[[5-(3-furanylmethylene)-4-methyl-3,6-dioxopiperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

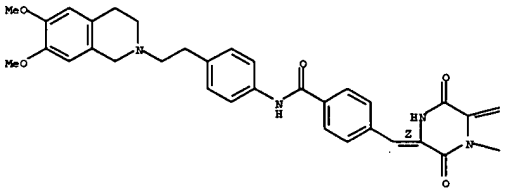
PAGE 1-B



RN 180598-25-9 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-4-[[5-(2-furanylmethylene)-4-methyl-3,6-dioxopiperazinylidene]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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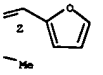
PAGE 1-B

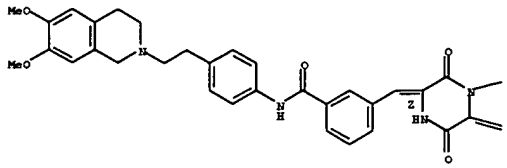


RN 180598-26-9 CAPLUS

CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-3-[[5-(2-furanylmethylene)-4-methyl-3,6-dioxopiperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

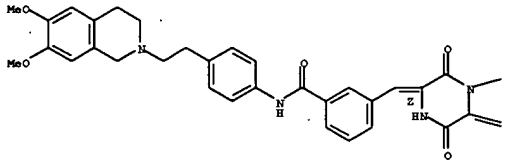


PAGE 1-B

RN 180598-27-0 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-3-[[5-(2-furanylmethylene)-4-methyl-3,6-dioxopiperazinylidene]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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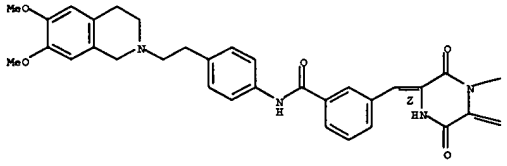
PAGE 1-A



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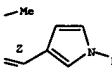

L7 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:188887 CAPLUS
DOCUMENT NUMBER: 124:261069
TITLE: Preparation of 3-(phenyl, 2-thienyl, and 2-furanyl)methylene-2,5-dioxopiperazine derivatives as inhibitors of plasminogen activator inhibitor
INVENTOR(S): Bryans, Justin Stephen; Folkes, Adrian John; Latham, Christopher John
PATENT ASSIGNEE(S): Xenova Ltd., UK
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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WO 9532190	A2	19951130	WO 1995-GB1180	19950524
WO 9532190	A3	19951214		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2190279	AA	19951130	CA 1995-2190279	19950524
AU 9525334	A1	19951218	AU 1995-25334	19950524
AU 688048	B2	19980305		
ZA 9504226	A	19960122	ZA 1995-4226	19950524
GB 2303851	A1	19970305	GB 1996-24251	19950524
GB 2303851	B2	19980506		

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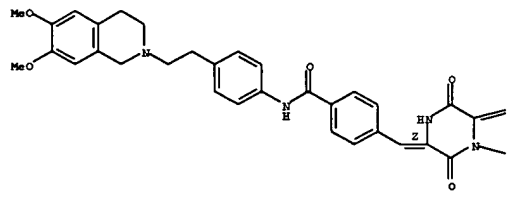
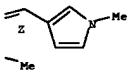
RN 180598-28-1 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-4-[[4-methyl-5-[(1-methyl-1H-pyrrol-3-yl)methylene]-3,6-dioxopiperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

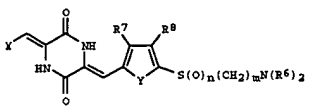


RN 180598-29-2 CAPLUS
CN Benzamide, N-[4-[2-(3,4-dihydro-6,7-dimethoxy-2(1H)-isoquinolinyl)ethyl]phenyl]-3-[[4-methyl-5-[(1-methyl-1H-pyrrol-3-yl)methylene]-3,6-dioxopiperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

EP 760812	A1	19970312	EP 1995-919549	19950524
R: DE, ES, FR, GB, IT, NL				
JP 10500425	T2	19980113	JP 1995-530151	19950524
US 5750530	A	19980512	US 1996-750020	19961217
PRIORITY APPLN. INFO.:			GB 1994-10387	A 19940524
			WO 1995-GB1180	W 19950524

OTHER SOURCE(S): MARPAT 124:261069
GI



I

AB Diketopiperazine derivs. [I; Y = CR9:CR10, O, S; R7, R8, R9, R10 = H, NO2; n = 0, 1 or 2; m = an integer of 1 to 6; each R6, which may be the same or different, is a C1-6 alkyl group; X = group selected from (1) (un)substituted Ph, (2) a heterocyclic ring selected from furan, thiophene, pyridine, quinoline and optionally C1-6 alkyl-substituted indole, (3) C1-C6 alkyl, 2,3-methylenedioxyphenyl, or 3,4-methylenedioxyphenyl, or (4) (CH2)pZ; wherein p = 0 or an integer of 1 to 4; Z = a cyclohexyl group substituted by one or more C1-C6 alkyl] and the salts and esters thereof, useful for the treatment of hemostatic disorders, thrombotic disorders, inflammation, and tumor growth and metastasis, are prepared Thus, 1.13 g 4-(2-dimethylaminoethylthio)benzaldehyde was added to a suspension of 1.14 g 1-acetyl-3-benzylidene-2,5-piperazinedione and 1.52 g Cs2CO3 in DMF and the resulting mixture was heated at 90° for 1 h, treated with H2O, and stirred overnight, and filtered to give, after recrystn. of the collected solid from MeOH/CH2Cl2, the title compound [(3Z,6Z)-II; R = H] in 62% yield. The HCl salt of latter compound and (3Z,6Z)-II.HCl (R = Cl) in vitro showed IC50 of 10.0 and 2.0 μM against plasminogen activator inhibitor.

IT 174766-07-5P 174766-08-6P 174766-20-2P
174766-23-5P 174766-27-9P 174766-28-0P
174766-29-1P 174766-30-4P 174766-31-5P
174766-32-6P 174766-34-8P 174766-35-9P
174766-36-0P 174766-37-1P 174766-38-2P
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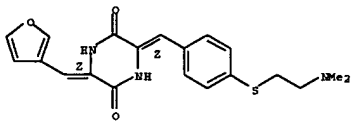
174850-02-3P 174850-03-4P 174850-04-5P
174850-06-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of [(Ph, thienyl, and furanyl]methylene]dioxopiperazine derivs. as inhibitors of plasminogen activator inhibitor)

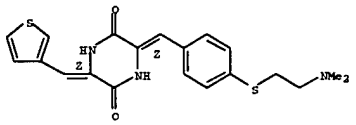
RN 174766-07-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethyl]thio]phenyl]methylene]-6-(3-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



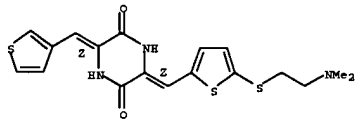
RN 174766-08-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethyl]thio]phenyl]methylene]-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



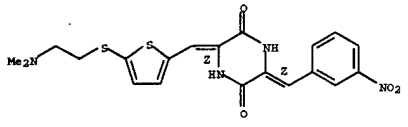
RN 174766-20-2 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



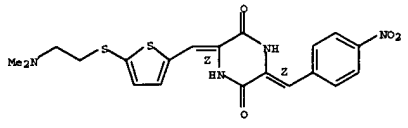
RN 174766-23-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(trifluoromethyl)phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



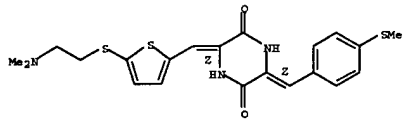
RN 174766-30-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-nitrophenyl)methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



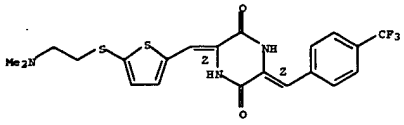
RN 174766-31-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(methylthio)phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



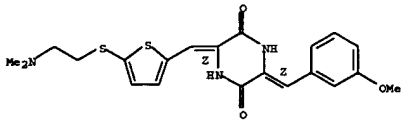
RN 174766-32-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(1,1-dimethylethyl)phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174766-27-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(3-methoxyphenyl)methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

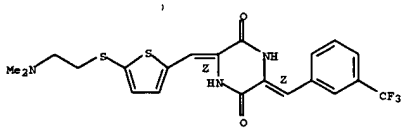
Double bond geometry as shown.



● HCl

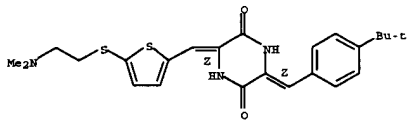
RN 174766-28-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[3-(trifluoromethyl)phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



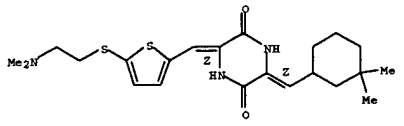
RN 174766-29-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(3-nitrophenyl)methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



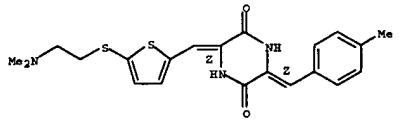
RN 174766-34-8 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(3,3-dimethylcyclohexyl)methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



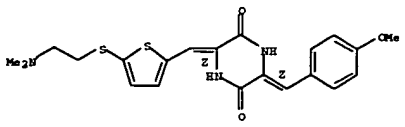
RN 174766-35-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-methylphenyl)methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



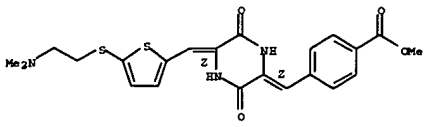
RN 174766-36-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-methoxyphenyl)methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174766-37-1 CAPLUS
CN Benzoic acid, 4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174766-38-2 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[3-methoxy-4-[(4-nitrophenyl)methoxy]phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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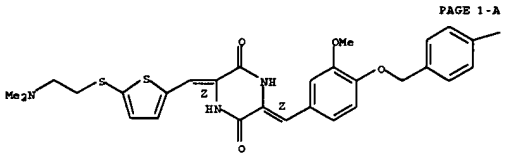
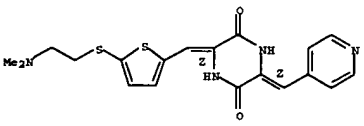


PAGE 1-B

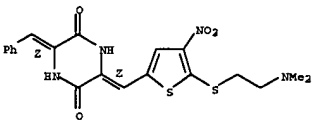
RN 174766-41-7 CAPLUS
CN 2-Thiophenecarboxamide, N-[4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]phenyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



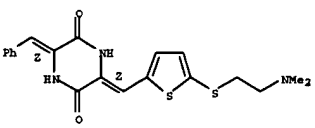
RN 174766-47-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-4-nitro-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174766-49-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (3Z,6Z)- (9CI) (CA INDEX NAME)

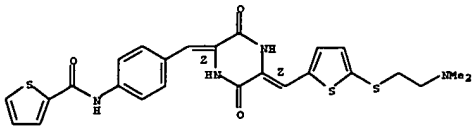
Double bond geometry as shown.



● HCl

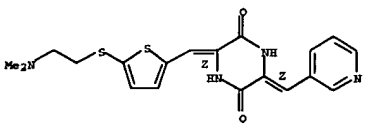
RN 174766-50-8 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(dimethylamino)phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



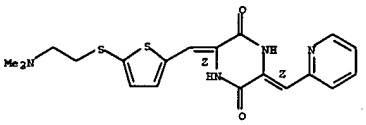
RN 174766-42-8 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(3-pyridinylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



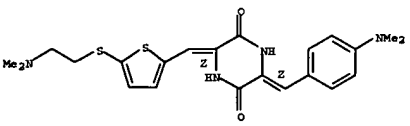
RN 174766-43-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(2-pyridinylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174766-44-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(4-pyridinylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

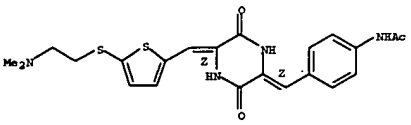
Double bond geometry as shown.



● HCl

RN 174766-51-9 CAPLUS
CN Acetamide, N-[4-[[5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]phenyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

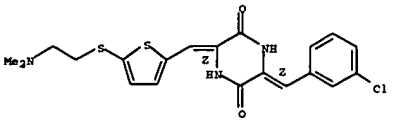
Double bond geometry as shown.



● HCl

RN 174766-52-0 CAPLUS
CN 2,5-Piperazinedione, 3-[(3-chlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

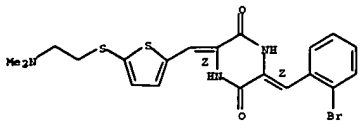
Double bond geometry as shown.



● HCl

RN 174766-53-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(2-bromophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

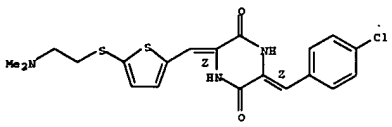
Double bond geometry as shown.



● HCl

RN 174766-54-2 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-chlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

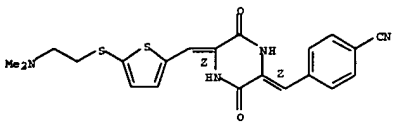
Double bond geometry as shown.



● HCl

RN 174766-55-3 CAPLUS
CN Benzonitrile, 4-[[5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

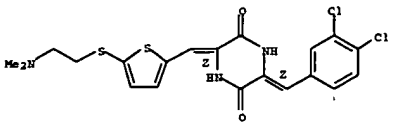
Double bond geometry as shown.



● HCl

RN 174766-56-4 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,4-dichlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

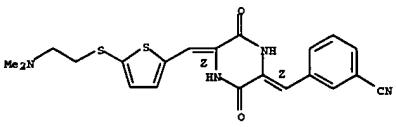
Double bond geometry as shown.



● HCl

RN 174766-57-5 CAPLUS
CN Benzonitrile, 3-[[5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

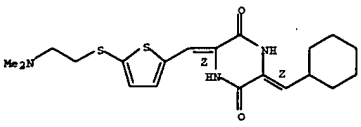
Double bond geometry as shown.



● HCl

RN 174766-58-6 CAPLUS
CN 2,5-Piperazinedione, 3-(cyclohexylmethylene)-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

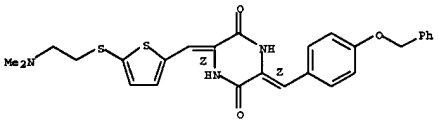
Double bond geometry as shown.



● HCl

RN 174766-59-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(phenylmethoxy)phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

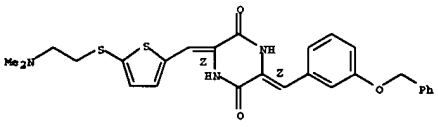
Double bond geometry as shown.



● HCl

RN 174766-60-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[3-(phenylmethoxy)phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

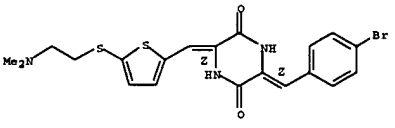
Double bond geometry as shown.



● HCl

RN 174766-61-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-bromophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

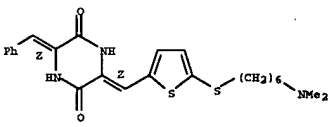
Double bond geometry as shown.



● HCl

RN 174766-63-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[6-(dimethylamino)hexyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

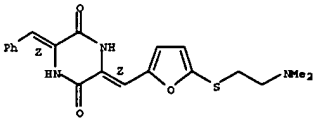
Double bond geometry as shown.



● HCl

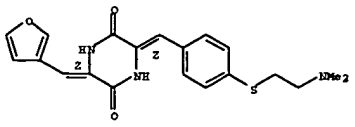
RN 174766-64-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-furanyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174849-59-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethyl]thio]phenyl]methylene]-6-(3-furanylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

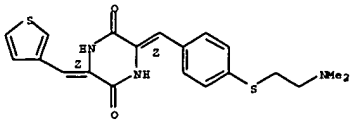
Double bond geometry as shown.



● HCl

RN 174849-60-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethyl]thio]phenyl]methylene]-6-(3-thienylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

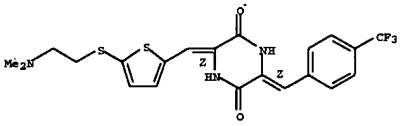
Double bond geometry as shown.



● HCl

RN 174849-72-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(trifluoromethyl)phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

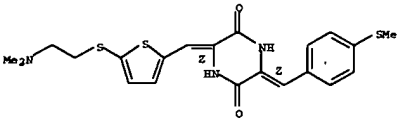
Double bond geometry as shown.



● HCl

RN 174849-75-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[3-(trifluoromethyl)phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

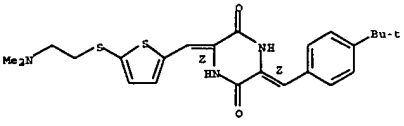
Double bond geometry as shown.



● HCl

RN 174849-79-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(1,1-dimethylethyl)phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

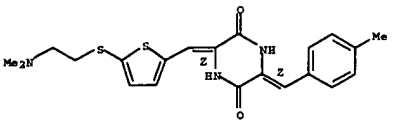
Double bond geometry as shown.



● HCl

RN 174849-80-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-methylphenyl)methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

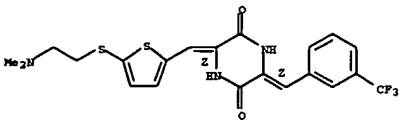
Double bond geometry as shown.



● HCl

RN 174849-81-1 CAPLUS

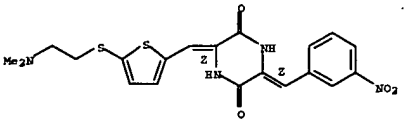
Double bond geometry as shown.



● HCl

RN 174849-76-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(3-nitrophenyl)methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

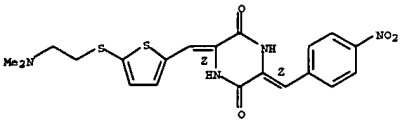
Double bond geometry as shown.



● HCl

RN 174849-77-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[(4-nitrophenyl)methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

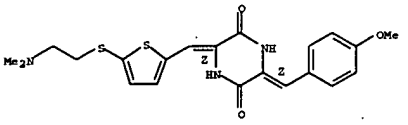


● HCl

RN 174849-78-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(methylthio)phenyl]methylene]-,

CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-methoxyphenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

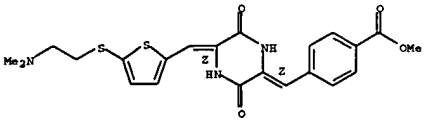
Double bond geometry as shown.



● HCl

RN 174849-82-2 CAPLUS
CN Benzoic acid, 4-[[5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]-, methyl ester, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

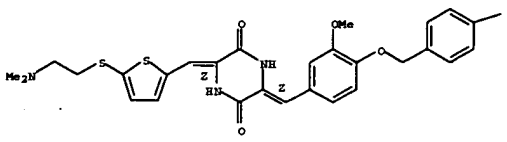
Double bond geometry as shown.



● HCl

RN 174849-83-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[3-methoxy-4-[(4-nitrophenyl)methoxy]phenyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

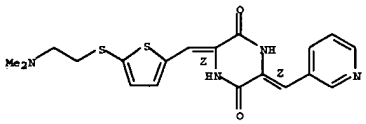


● HCl

NO_2

RN 174849-86-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(3-pyridinylmethylene)-, monohydrochloride, (Z,Z)-(9CI) (CA INDEX NAME)

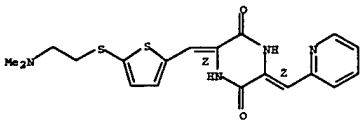
Double bond geometry as shown.



● HCl

RN 174849-87-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(2-pyridinylmethylene)-, monohydrochloride, (Z,Z)-(9CI) (CA INDEX NAME)

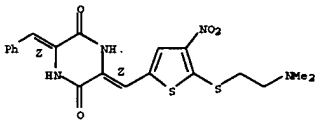
Double bond geometry as shown.



● HCl

RN 174849-90-2 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-4-nitro-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

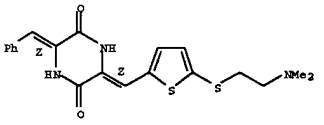
Double bond geometry as shown.



● HCl

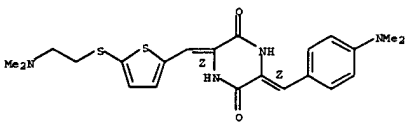
RN 174849-92-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



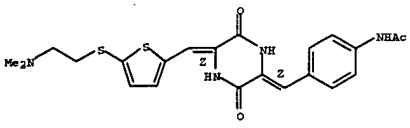
RN 174849-93-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(dimethylamino)phenyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



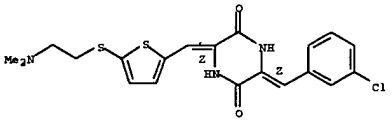
RN 174849-94-6 CAPLUS
CN Acetamide, N-[4-[[5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]phenyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



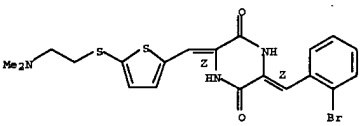
RN 174849-95-7 CAPLUS
CN 2,5-Piperazinedione, 3-[(3-chlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



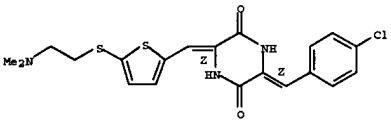
RN 174849-96-8 CAPLUS
CN 2,5-Piperazinedione, 3-[(2-bromophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



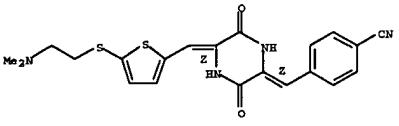
RN 174849-97-9 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-chlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



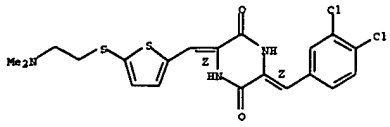
RN 174849-98-0 CAPLUS
CN Benzonitrile, 4-[(Z)-[(5Z)-5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



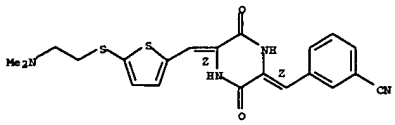
RN 174849-99-1 CAPLUS
CN 2,5-Piperazinedione, 3-[(3,4-dichlorophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



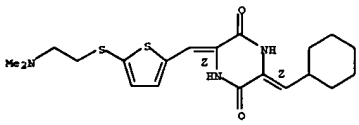
RN 174850-00-1 CAPLUS
CN Benzonitrile, 3-[[5-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-3,6-dioxopiperazinylidene]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



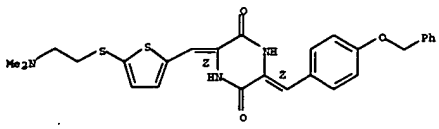
RN 174850-01-2 CAPLUS
CN 2,5-Piperazinedione, 3-(cyclohexylmethylene)-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



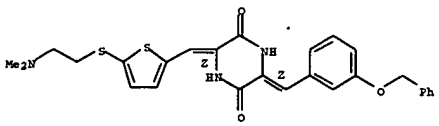
RN 174850-02-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[4-(phenylmethoxy)phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



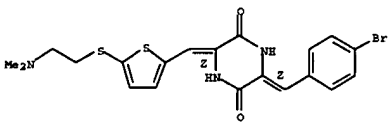
RN 174850-03-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-6-[[3-(phenylmethoxy)phenyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



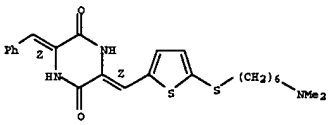
RN 174850-04-5 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-bromophenyl)methylene]-6-[[5-[[2-(dimethylamino)ethyl]thio]-2-thienyl]methylene]-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 174850-06-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[6-(dimethylamino)hexyl]thio]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

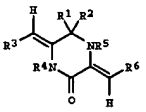
Double bond geometry as shown.



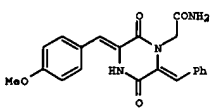
L7 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:994199 CAPLUS
DOCUMENT NUMBER: 124:55981
TITLE: Preparation of 3,6-bis(benzylidene)piperazine-2,5-diones as multidrug resistance modulators
INVENTOR(S): Bryans, Justin Stephen; Latham, Christopher John; Brocchini, Stephen James
PATENT ASSIGNEE(S): Xenova Ltd., UK
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9521830	A1	19950817	WO 1995-GB300		19950214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UG, US, UZ, VN					
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
GB 2286394	A1	19950816	GB 1995-2872		19950214
GB 2286394	B2	19980812			
AU 9515884	A1	19950829	AU 1995-15884		19950214
ZA 9501181	A	19960814	ZA 1995-1181		19950214
US 5852018	A	19981222	US 1996-693171		19961104
PRIORITY APPLN. INFO.:			GB 1994-2809	A	19940214
			WO 1995-GB300	W	19950214

OTHER SOURCE(S): MARPAT 124:55981
GI



I



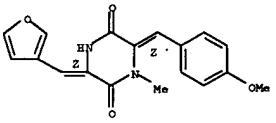
II

AB Title compds. [I; R1 = OR7 and R2R5 = bond; R1R2 = O and R5 = H, (un)substituted alkyl; R3,R6 = (un)substituted Ph; R4 = H, (un)substituted alkyl; R7 = (un)substituted alkyl] were prepared Title compound II (concentration not given) gave daunorubicin uptake by multidrug resistant EMT6 mouse mammary carcinoma subline AR 1.0 cells 73.9% that of verapamil at 100μM.

IT 171722-48-8P 171722-49-9P 171722-50-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3,6-bis(benzylidene)piperazine-2,5-diones as multidrug resistance modulators)

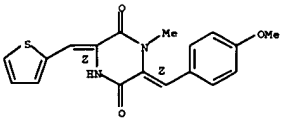
RN 171722-48-8 CAPLUS
CN 2,5-Piperazinedione, 3-(3-furanylmethylene)-6-[(4-methoxyphenyl)methylene]-1-methyl-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



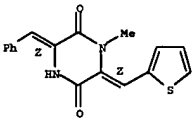
RN 171722-49-9 CAPLUS
CN 2,5-Piperazinedione, 6-[(4-methoxyphenyl)methylene]-1-methyl-3-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171722-50-2 CAPLUS
CN 2,5-Piperazinedione, 1-methyl-3-(phenylmethylene)-6-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

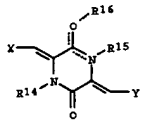


L7 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:994198 CAPLUS
DOCUMENT NUMBER: 124:55980
TITLE: Preparation of piperazinedione-derivative multiple drug resistance modulators
INVENTOR(S): Brocchini, Stephen James; Bryans, Justin Stephen; Latham, Christopher John; Folkes, Adrian John
PATENT ASSIGNEE(S): Xenova Ltd., UK
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9521831	A1	19950817	WO 1995-GB301	19950214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
GB 2286392	A1	19950816	GB 1995-2860	19950214
GB 2286392	B2	19980812		
AU 9516676	A1	19950829	AU 1995-16676	19950214
ZA 9501175	A	19960814	ZA 1995-1175	19950214
US 5861400	A	19990119	US 1996-693169	19961104
PRIORITY APPLN. INFO.:			GB 1994-2805 A	19940214
			WO 1995-GB301 W	19950214

OTHER SOURCE(S): MARPAT 124:55980

GI



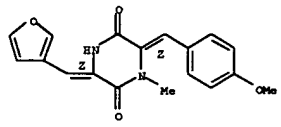
I

AB The title compds. [I; the dotted line represents an optional double bond; R14 = H, Ph-(un)substituted C1-6 alkyl; R15 = H, C1-6 alkyl; R16 = (un)substituted C1-6 alkyl; X, Y = (un)substituted heterocyclic ring, (un)substituted Ph, cyclohexyl, etc.], useful as modulators of multiple drug resistance, are prepared and a 1-containing formulation presented. Thus, (3Z,6Z)-3-benzylidene-1,4-dimethyl-6-(1-tert-butoxycarbonyl-3-indolyl)methylene-2,5-piperazinedione (II) was prepared and demonstrated a potentiation index for doxorubicin of 40 (i.e., IC50 for doxorubicin alone/IC50 for doxorubicin and II) of 40 against EMT6 mouse mammary carcinoma cell line AR 1.0 cells.

IT 171722-48-8P 171722-49-9P 171722-50-2P
171871-85-5P 171871-86-6P 171871-87-7P
171871-89-9P 171871-92-4P 171871-93-5P
171871-94-6P 171871-99-1P 171872-00-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinedione-derivative multiple drug resistance modulators)

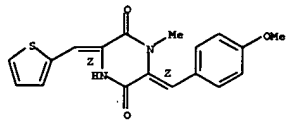
RN 171722-48-8 CAPLUS
CN 2,5-Piperazinedione, 3-(3-furanylmethylene)-6-[(4-methoxyphenyl)methylene]-1-methyl-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



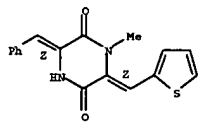
RN 171722-49-9 CAPLUS
CN 2,5-Piperazinedione, 6-[(4-methoxyphenyl)methylene]-1-methyl-3-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



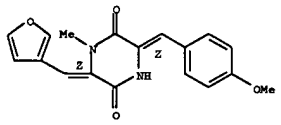
RN 171722-50-2 CAPLUS
CN 2,5-Piperazinedione, 1-methyl-3-(phenylmethylene)-6-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171871-85-5 CAPLUS
CN 2,5-Piperazinedione, 6-(3-furanylmethylene)-3-[(4-methoxyphenyl)methylene]-1-methyl-, (Z,Z)- (9CI) (CA INDEX NAME)

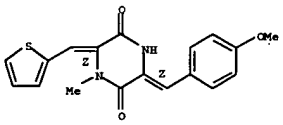
Double bond geometry as shown.



RN 171871-86-6 CAPLUS

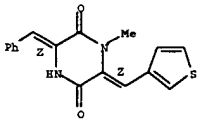
CN 2,5-Piperazinedione, 3-[(4-methoxyphenyl)methylene]-1-methyl-6-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



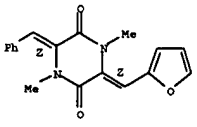
RN 171871-87-7 CAPLUS
CN 2,5-Piperazinedione, 1-methyl-3-(phenylmethylene)-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



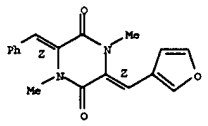
RN 171871-89-9 CAPLUS
CN 2,5-Piperazinedione, 3-(2-furanylmethylene)-1,4-dimethyl-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



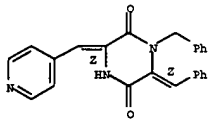
RN 171871-92-4 CAPLUS
CN 2,5-Piperazinedione, 3-(3-furanylmethylene)-1,4-dimethyl-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



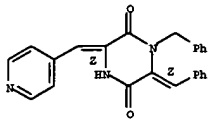
RN 171871-93-5 CAPLUS
CN 2,5-Piperazinedione, 1-(phenylmethyl)-6-(phenylmethylene)-3-(4-pyridinylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171871-94-6 CAPLUS
CN 2,5-Piperazinedione, 1-(phenylmethyl)-6-(phenylmethylene)-3-(4-pyridinylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

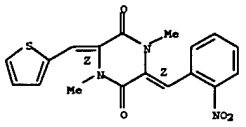
Double bond geometry as shown.



● HCl

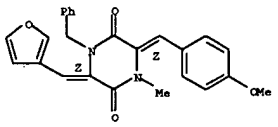
RN 171871-99-1 CAPLUS
CN 2,5-Piperazinedione, 1,4-dimethyl-3-[(2-nitrophenyl)methylene]-6-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171872-00-7 CAPLUS
CN 2,5-Piperazinedione, 3-[3-furanylmethylene]-6-[[4-methoxyphenyl]methylene]-1-methyl-4-(phenylmethyl)-, (Z,Z)- (9CI) (CA INDEX NAME)

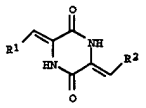
Double bond geometry as shown.



L7 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:994197 CAPLUS
DOCUMENT NUMBER: 124:55979
TITLE: Preparation of piperazinedione-derivative inhibitors of plasminogen activator inhibitor
INVENTOR(S): Brocchini, Stephen James; Bryans, Justin Stephen; Folkes, Adrian John; Latham, Christopher John; Brumwell, Julie Elizabeth
PATENT ASSIGNEE(S): Xenova Ltd., UK
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9521832	A1	19950817	WO 1995-GB302	19950214
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
GB 2286395	A1	19950816	GB 1995-2874	19950214
GB 2286395	B2	19980826		
CA 2182877	AA	19950817	CA 1995-2182877	19950214
AU 9516677	A1	19950829	AU 1995-16677	19950214
AU 693159	B2	19980625		
ZA 9501180	A	19960814	ZA 1995-1180	19950214
EP 745070	A1	19961204	EP 1995-908314	19950214
R: DE, ES, FR, GB, IT, NL				
JP 09509157	T2	19970916	JP 1995-521082	19950214
US 5891877	A	19990406	US 1996-693172	19960925
PRIORITY APPLN. INFO.:			GB 1994-2807	A 19940214
			WO 1995-GB302	W 19950214

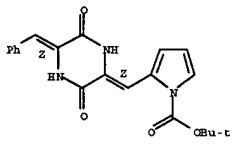
OTHER SOURCE(S): MARPAT 124:55979
GI



I

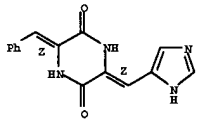
AB The title compds. [I; R1, R2 = (un)substituted naphthyl, (un)substituted (un)saturated heterocyclyl, (un)substituted Ph, (un)substituted cyclohexyl, etc.], which have activity as inhibitors of plasminogen activator inhibitor (PAI), are prepared and a I-containing formulation is presented. Thus, (3Z,6Z)-3-benzylidene-6-[4-(2-imidazolylethoxy)benzylidene]-3,5-piperazinedione was prepared and demonstrated a IC50 in a chromogenic PAI substrate assay (K. Nilsson, 1987) of 5.0-10.0 μM.
IT 171887-10-8P 171887-16-4P 171887-17-5P
171887-26-6P 171887-27-7P 171887-29-9P
171887-33-5P 171887-40-4P 171887-41-5P
171887-42-6P 171887-43-7P 171887-44-8P
171887-45-9P 171887-46-0P 171887-47-1P
171887-48-2P 171887-49-3P 171887-50-6P
171887-51-7P 171887-53-9P 171887-54-0P
171887-55-1P 171887-61-9P 171887-62-0P
171887-63-1P 171887-64-2P 171887-65-3P
171887-66-4P 171887-71-1P 171887-72-2P
171887-73-3P 171887-74-4P 171887-76-6P
171887-77-7P 171887-78-8P 171887-84-6P
171887-85-7P 171887-86-8P 171887-88-0P
171887-89-1P 171887-90-4P 171887-91-5P
171887-92-6P 171887-93-7P 171888-00-9P
171888-01-0P 171888-24-7P 171888-28-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperazinedione-derivative inhibitors of plasminogen activator inhibitor)
RN 171887-10-8 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-[[3,6-dioxo-5-(phenylmethylene)piperazinylidene]methyl]-, 1,1-dimethylethyl ester, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



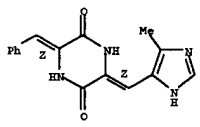
RN 171887-16-4 CAPLUS
CN 2,5-Piperazinedione, 3-(1H-imidazol-4-ylmethylene)-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



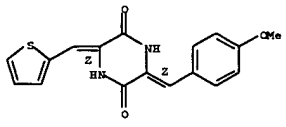
RN 171887-17-5 CAPLUS
CN 2,5-Piperazinedione, 3-[(5-methyl-1H-imidazol-4-yl)methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



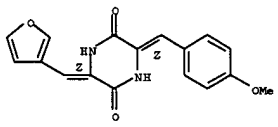
RN 171887-26-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-methoxyphenyl)methylene]-6-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



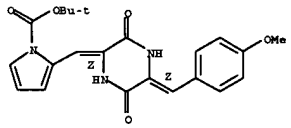
RN 171887-27-7 CAPLUS
CN 2,5-Piperazinedione, 3-(3-furanylmethylene)-6-[(4-methoxyphenyl)methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



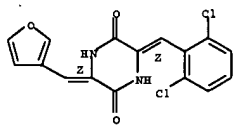
RN 171887-29-9 CAPLUS
CN 1H-Pyrrole-1-carboxylic acid, 2-[[5-[(4-methoxyphenyl)methylene]-3,6-dioxopiperazinylidene]methyl]-, 1,1-dimethylethyl ester, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



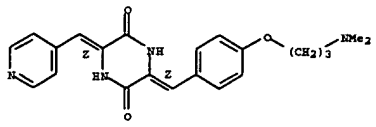
RN 171887-33-5 CAPLUS
CN 2,5-Piperazinedione, 3-[(2,6-dichlorophenyl)methylene]-6-(3-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



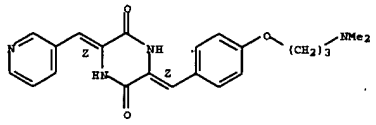
RN 171887-40-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(4-pyridinylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



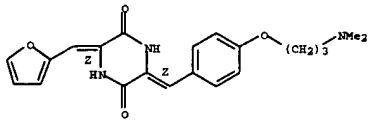
RN 171887-41-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(3-pyridinylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



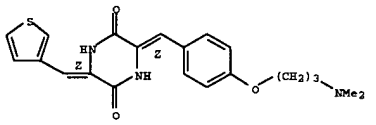
RN 171887-42-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(2-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

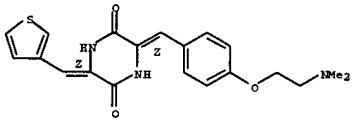


RN 171887-43-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

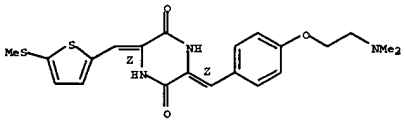


RN 171887-44-8 CAPLUS



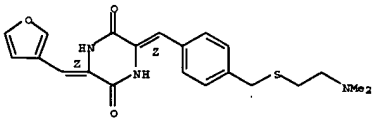
RN 171887-46-2 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]phenyl]methylene]-6-[[5-(methylthio)-2-thienyl]methylene]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



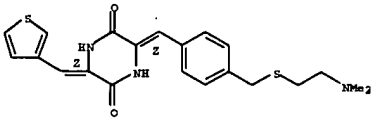
RN 171887-49-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[[2-(dimethylamino)ethyl]thio]methyl]phenyl]methylene]-6-(3-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171887-50-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[[2-(dimethylamino)ethyl]thio]methyl]phenyl]methylene]-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME).

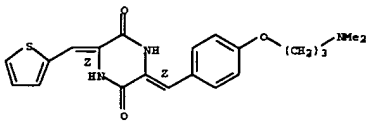
Double bond geometry as shown.



RN 171887-51-7 CAPLUS

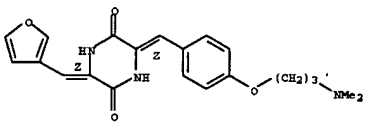
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(2-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



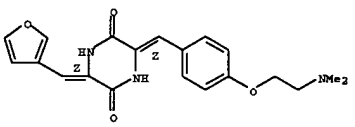
RN 171887-45-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(3-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171887-46-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]phenyl]methylene]-6-(3-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

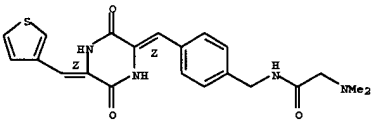


RN 171887-47-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]phenyl]methylene]-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

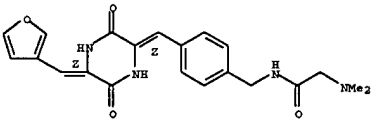
CN Acetamide, 2-(dimethylamino)-N-[[4-[[3,6-dioxo-5-(3-thienylmethylene)piperazinylidene]methyl]phenyl]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



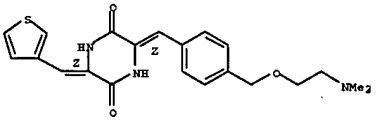
RN 171887-53-9 CAPLUS
CN Acetamide, 2-(dimethylamino)-N-[[4-[[5-(3-furanylmethylene)-3,6-dioxopiperazinylidene]methyl]phenyl]methyl]-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



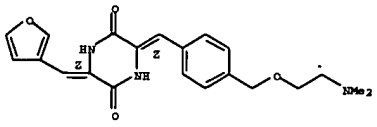
RN 171887-54-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethoxy]methyl]phenyl]methylene]-6-(3-thienylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



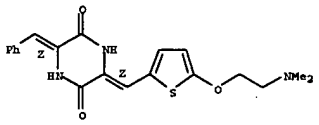
RN 171887-55-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethoxy]methyl]phenyl]methylene]-6-(3-furanylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



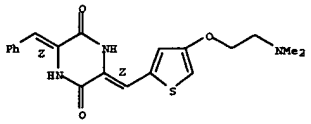
RN 171887-61-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[2-(dimethylamino)ethoxy]-2-thienyl]methylene]-6-(phenylmethylene)-, (3Z,6Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



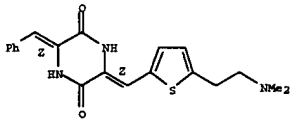
RN 171887-62-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

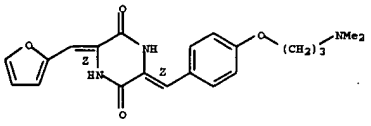


RN 171887-63-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[2-(dimethylamino)ethyl]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



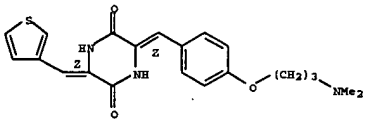
RN 171887-64-2 CAPLUS



● HCl

RN 171887-72-2 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(3-thienylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

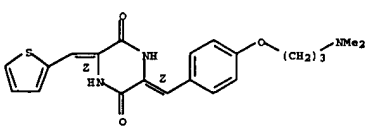
Double bond geometry as shown.



● HCl

RN 171887-73-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(2-thienylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



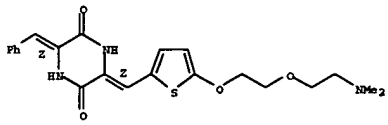
● HCl

RN 171887-74-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(3-furanylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

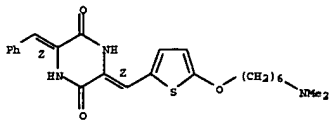
CN 2,5-Piperazinedione, 3-[[5-[2-[2-(dimethylamino)ethoxy]ethoxy]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



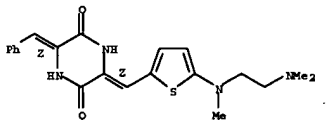
RN 171887-65-3 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[6-(dimethylamino)hexyl]oxy]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



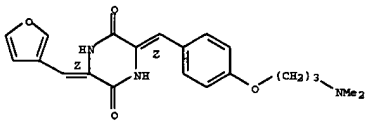
RN 171887-66-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[2-(dimethylamino)ethyl]methylamino]-2-thienyl]methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 171887-71-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(2-furanylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

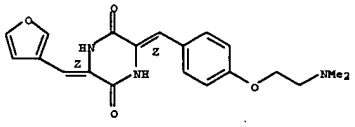
Double bond geometry as shown.



● HCl

RN 171887-76-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]phenyl]methylene]-6-(3-furanylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

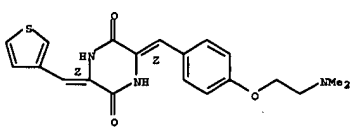
Double bond geometry as shown.



● HCl

RN 171887-77-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]phenyl]methylene]-6-(3-thienylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

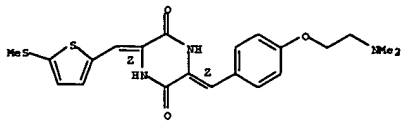
Double bond geometry as shown.



● HCl

RN 171887-78-8 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[2-(dimethylamino)ethoxy]phenyl]methylene]-6-[[5-(methylthio)-2-thienyl]methylene]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

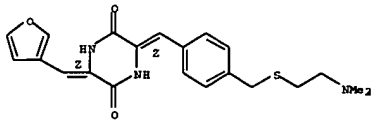
Double bond geometry as shown.



● HCl

RN 171887-84-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[[2-(dimethylamino)ethyl]thio]methyl]phenyl]methylene]-6-(3-furanylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

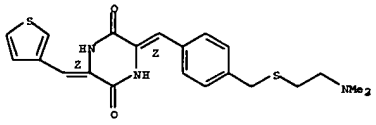
Double bond geometry as shown.



● HCl

RN 171887-85-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[[2-(dimethylamino)ethyl]thio]methyl]phenyl]methylene]-6-(3-thienylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

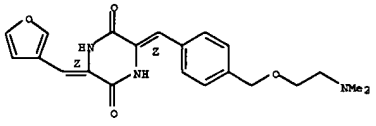
Double bond geometry as shown.



● HCl

RN 171887-86-8 CAPLUS
CN Acetamide, 2-(dimethylamino)-N-[[4-[[3,6-dioxo-5-(3-thienylmethylene)piperazinylidene]methyl]phenyl]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

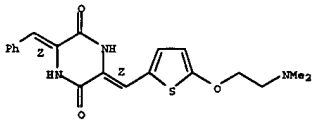
Double bond geometry as shown.



● HCl

RN 171887-91-5 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[2-(dimethylamino)ethoxy]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

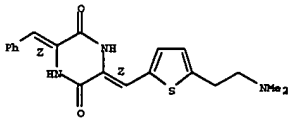
Double bond geometry as shown.



● HCl

RN 171887-92-6 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[2-(dimethylamino)ethyl]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

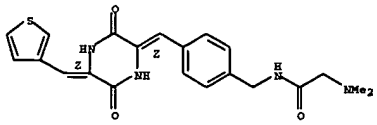
Double bond geometry as shown.



● HCl

RN 171887-93-7 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[[6-(dimethylamino)hexyl]oxy]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (Z,Z)- (9CI)

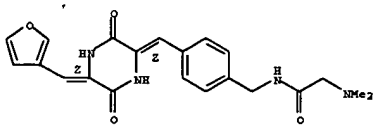
Double bond geometry as shown.



● HCl

RN 171887-88-0 CAPLUS
CN Acetamide, 2-(dimethylamino)-N-[[4-[[5-(3-furanylmethylene)-3,6-dioxopiperazinylidene]methyl]phenyl]methyl]-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

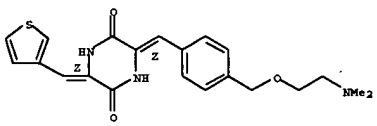
Double bond geometry as shown.



● HCl

RN 171887-89-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethoxy]methyl]phenyl]methylene]-6-(3-thienylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

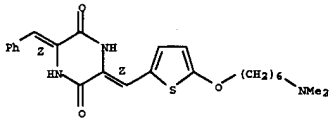
Double bond geometry as shown.



● HCl

RN 171887-90-4 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[[2-(dimethylamino)ethoxy]methyl]phenyl]methylene]-6-(3-furanylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

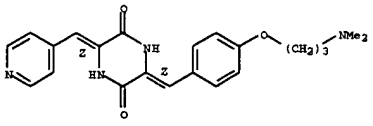
Double bond geometry as shown.



● HCl

RN 171888-00-9 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(4-pyridinylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

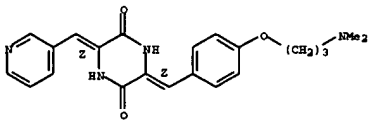
Double bond geometry as shown.



● HCl

RN 171888-01-0 CAPLUS
CN 2,5-Piperazinedione, 3-[[4-[3-(dimethylamino)propoxy]phenyl]methylene]-6-(3-pyridinylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

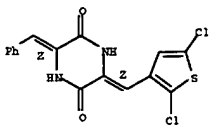
Double bond geometry as shown.



● HCl

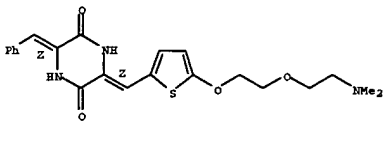
RN 171888-24-7 CAPLUS
CN 2,5-Piperazinedione, 3-[(2,5-dichloro-3-thienyl)methylene]-6-(phenylmethylene)-, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



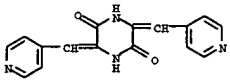
RN 171888-28-1 CAPLUS
CN 2,5-Piperazinedione, 3-[[5-[2-[2-(dimethylamino)ethoxy]ethoxy]-2-thienyl]methylene]-6-(phenylmethylene)-, monohydrochloride, (Z,Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

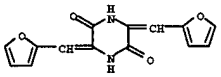


● HCl

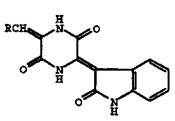
L7 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:864144 CAPLUS
DOCUMENT NUMBER: 124:55901
TITLE: Novel bis-(N-alkyl-N,N-dimethylammonium) polyetheneglycol ether salts as phase transfer catalysts in the condensation of 1,4-diacetyl-2,5-piperazinedione and aldehydes
AUTHOR(S): Wang, Li-xin; Yu, Ming-hua; Shi, Yao-zeng; Hu, Hong-wen
CORPORATE SOURCE: Department of Chemistry, Nanjing University, Nanjing, 210008, Peop. Rep. China
SOURCE: Chemical Research in Chinese Universities (1995), 11(2), 178-84
CODEN: CRCUED; ISSN: 1000-9213
PUBLISHER: Higher Education Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of bis-(N-alkyl-N,N-dimethylammonium) polyetheneglycol ether salts as phase transfer catalysts for the condensation reaction of 1,4-diacetyl-2,5-piperazinedione with aldehydes was reported. A example catalyst is 2,2'-oxybis[N,N,N-trimethylethanaminium] dichloride.
IT **114932-14-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 114932-14-8 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-furanylmethylene)- (9CI) (CA INDEX NAME)



RN 114932-14-8 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-furanylmethylene)- (9CI) (CA INDEX NAME)

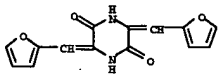


L7 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:630947 CAPLUS
DOCUMENT NUMBER: 109:230947
TITLE: Conjugated systems derived from piperazine-2,5-dione
AUTHOR(S): Katritzky, Alan R.; Fan, Wei Qiang; Szajda, Maria; Li, Qiao Ling; Caster, Kenneth C.
CORPORATE SOURCE: Dep. Chem., Univ. Florida, Gainesville, FL, 32611, USA
SOURCE: Journal of Heterocyclic Chemistry (1988), 25(2), 591-7
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:230947
GI

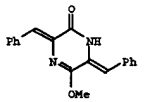


I

AB The preparation of mono- and of sym. and unsym. bis-ylidine derivs. of piperazine-2,5-dione is described. The UV-visible absorption of indolylidene derivs. I (R = 4-R1C6H4, 3-ClC6H4, 2-pyridyl, 4-pyridyl; R1 = H, Me, MeO, NO2) is correlated with acceptor/donor character of the substituents.
IT **7670-69-1P 114912-62-8P 117563-27-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and condensation reaction of, with chloroindolone or nitrobenzaldehyde)
RN 7670-69-1 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)

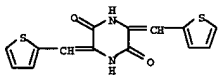


L7 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:417408 CAPLUS
DOCUMENT NUMBER: 113:17408
TITLE: Neihumicin, a new cytotoxic antibiotic from Micromonospora neihuensis
AUTHOR(S): Wu, Rong Yang; Yang, Li Ming; Yokoi, T.; McPhail, A. T.; Yokoi, T.; Lee, Kuo Hsiung
CORPORATE SOURCE: Inst. Bot., Acad. Sin., Taipei, Taiwan
SOURCE: Zhongyang Yanjiuyuan Zhiwu Yanjiuso Zhuankan (1989), 8(Chih Wu Fen Tzu Sheng Wu Hsueh), 19-40
CODEN: CYCKDV; ISSN: 0258-5170
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI

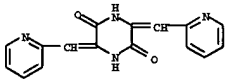


I

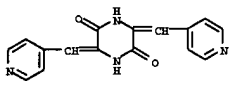
AB Neihumicin (I) isolated from a culture of M. neihuensis showed cytotoxic activity against KB cells (ED50 0.94 μg/mL) and microbicidal activity against Saccharomyces cerevisiae. The piperazine-2,5-dione present was essential for its cytotoxic activity. The analogs of I were also prepared, and they also showed cytotoxicity.
IT **105975-15-3P 114912-62-8P 114932-14-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antitumor activity of)
RN 105975-15-3 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-thienylmethylene)- (9CI) (CA INDEX NAME)



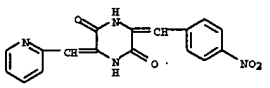
RN 114912-62-8 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(4-pyridinylmethylene)- (9CI) (CA INDEX NAME)



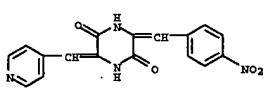
RN 114912-62-8 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(4-pyridinylmethylene)- (9CI) (CA INDEX NAME)



RN 117563-27-6 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-nitrophenyl)methylene]-6-(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)

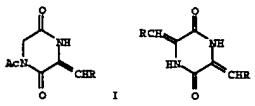


IT **117563-28-7P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and visible spectra of)
RN 117563-28-7 CAPLUS
CN 2,5-Piperazinedione, 3-[(4-nitrophenyl)methylene]-6-(4-pyridinylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:416593 CAPLUS
DOCUMENT NUMBER: 109:16593
TITLE: Neihumicin, a new cytotoxic antibiotic from Micromonospora neihuensis. III. Structure-activity relationships
AUTHOR(S): Yokoi, Toshio; Yang, Li Ming; Yokoi, Tomiko; Wu, Rong Yang; Lee, Kuo Hsiung
CORPORATE SOURCE: Sch. Pharm., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SOURCE: Journal of Antibiotics (1988), 41(4), 494-501
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 109:16593
GI

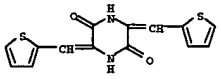


I II

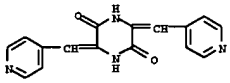
AB Structure-cytotoxicity relations indicated that the C-3 [I, R = Ph, C6H5-n(OMe)n (n = 1-3) or pyridyl] and C-6 [II, R = toluyl, chlorophenyl, C6H5-n(OMe)n (n = 2 or 3), pyridyl, Ph, furyl or thienyl] disubstituted piperazine-2,5-diones are structurally required for significant cytotoxicity, and the neihumicin-like C-3 and C-6 disubstituted unsym. piperazine derivs. are, in general, more cytotoxic than the corresponding sym. piperazine-2,5-diones. Several synthetic analogs including 3,6-di-(2,4,5-trimethoxybenzylidene)piperazine-2,5-dione, 3,6-dibenzylidene-2-ethoxy-3,6-dihydropyrazin-5-one, 3-benzylidene-6-(m-chlorobenzylidene)-2-methoxy-3,6-dihydropyrazin-5-one, and 3,6-bis(m-chlorobenzylidene)-2-methoxy-3,6-dihydropyrazin-5-one, were prepared and shown to be more cytotoxic than neihumicin.

IT **105975-15-3P 114912-62-8P 114932-14-8P**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and cytotoxicity of)

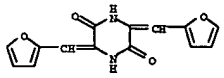
RN 105975-15-3 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-thienylmethylene)- (9CI) (CA INDEX NAME)



RN 114912-62-8 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(4-pyridinylmethylene)- (9CI) (CA INDEX NAME)



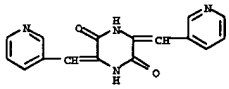
RN 114932-14-8 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-furanylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:67610 CAPLUS
DOCUMENT NUMBER: 78:67610
TITLE: Potential hypolipidemic agents. III. Heterocyclic compounds affecting free fatty acid mobilization in vivo
AUTHOR(S): Carlson, Lars A.; Hedbom, Christina; Helgstrand, Erik; Sjoberg, Berndt; Stjernstrom, Nils E.
CORPORATE SOURCE: King Gustaf Vth Res. Inst., Stockholm, Swed.
SOURCE: Acta Pharmaceutica Suecica (1972), 9(4), 289-304
CODEN: APSXAS; ISSN: 0001-6675
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Compds. such as 3-methyl-5-isoxazolecarboxylic acid [4857-42-5], 5-fluoronicotinic acid [402-66-4], 5-fluoro-3-pyridylacetic acid [38129-24-7], and 3-methylpyrazole [1453-58-3] exhibited the highest inhibition of free fatty acid mobilization in blood among 188 heterocyclic compds. tested in dogs, while compds. such as 5-methyl-3-isoxazolecarboxylic acid [3405-77-4], 2-fluoronicotinic acid [393-55-5], and 3-aminobenzoic acid [99-05-8] had no effect on free fatty acid mobilization.

IT **41668-18-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(lipid metabolism inhibition by)

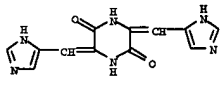
RN 41668-18-2 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(3-pyridinylmethylene)- (9CI) (CA INDEX NAME)



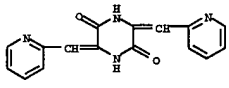
L7 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:490652 CAPLUS
DOCUMENT NUMBER: 65:90652
ORIGINAL REFERENCE NO.: 65:16969a-f
TITLE: 2,5-Dioxopiperazines. II. Reaction of 2,5-dioxopiperazine with aldehydes and nitroso compounds
AUTHOR(S): Augustin, Manfred
CORPORATE SOURCE: Martin-Luther-Univ., Halle, Germany
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1966), 32(3-4), 158-66
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: German
AB cf. CA 61, 7014g; 64, 17707g. Aldehydes containing a grouping capable of polarizing the C:O group can react with 2,5-dioxopiperazine (I) in H2O-extracting solvents. The strongly neg. O atom takes up a proton from the active CH2 group of I to leave a free electron pair in the ring system which forms a C-C bond with the electrophilic C atom of the aldehyde. Loss of H2O then results in the formation of a double bond. Nitroso compds. behaved similarly. Finely powdered I (0.05 mole) was mixed with 0.1 mole aldehyde or nitroso compound, 15 g. H2O-free AcONa, and 25 g. Ac2O, the mixture heated 3 hrs. at 130-40° in an oil-bath and cooled, hot H2O added, and when cold the aqueous phase filtered to remove insol. material. The residual resin was treated with hot EtOH and the precipitate boiled several times with EtOH. Recrystn. from glacial AcOH or precipitation with H2O from a glacial AcOH solution usually gave high melting amorphous powders. In this way the following new substituted 2,5-dioxopiperazines were obtained (starting material, substituents, % yield, and m.p. given): salicylaldehyde, 3,6-bis(2-acetoxybenzylidene) 251-5° (decomposition) (glacial AcOH); m-hydroxybenzaldehyde, 3,6-bis(3-acetoxybenzylidene), 273° (decomposition); 2,5-dihydroxybenzaldehyde, 3,6-bis(2,5-diacetoxybenzylidene), 57, 220-2° (decomposition); m-nitrobenzaldehyde, 3,6-bis(3-nitrobenzylidene) (yellowish brown), 74.5, 255° (decomposition); o-nitrobenzaldehyde, 3,6-bis(2nitrobenzylidene) (yellow), 58, 165° (decomposition); p-nitrobenzaldehyde, 3,6-bis(4-nitrobenzylidene) (yellow), 63, 140-2°; o-chlorobenzaldehyde, 3,6-bis(2-chlorobenzylidene), 67, 187-90° p-iodobenzaldehyde, 3,6-bis(4-iodobenzylidene), 59, 223° (decomposition), p-cyanobenzaldehyde, 3,6-bis(4-cyanobenzylidene), 66.5, 240-2°, imidazole-4(5)-carboxaldehyde, 3,6-bis(4(5)-imidazolylmethylene) (yellow), 52, decomposed 270°; 2-pyridinecar- boxaldehyde, 3,6-bis(2-pyridylmethylene) (dark crystals), 41, did not decompose 300° 2,2,2-tribromoacetaldehyde, 3,6-bis(2,2,2-tribromoethylidene), (dark powder), 31, decomposed 249°; 2,2-bis(p-methoxyphenyl)acetaldehyde, 3,6-bis[2,2-bis(p-methoxyphenyl)ethylidene, 51, 127°, crotonaldehyde, 3,6-bis(butyl-1,3-diene) (yellowish-brown), 55, 222-5°; cinnamaldehyde, 3,6-dicinnamylidene (orange-yellow), 52, decomposed 270°; nitrosobenzene, 3,6-bis(phenylimino) (black), 42, did not decompose 300°; o-nitrosophenol, 3,6-bis(2-acetoxyphenylimino) (black) 44.5, did not decompose 300°; 1-nitroso-2-naphthol, 3,6-bis(2-acetoxy-1-naphthylimino) (black), did not decompose 300°; p-nitrosodimeth- ylaniline, 3,6-bis[(p-dimethylaminophenyl)imino] (dark powder), 53, 218° (decomposition). Some benzylidene compds. were also reduced to the corresponding benzyl derivs. The benzylidene compound (2 g.) was added to 100 ml. boiling glacial AcOH and 5 g. Zn dust added a little at a time. After refluxing for 12 hrs., the mixture was filtered hot. A crystalline mass separated on cooling; this was washed with cold H2O and crystallized from glacial AcOH or precipitated from a concentrated glacial AcOH solution with H2O to give the following substituted 2,5-dioxopiperazines (substituents, % yield, and m.p. given): 3,6-bis(2-acetoxybenzyl), 74.5, 230-5° (decomposition); 3,6-bis(2-chlorobenzyl), 74, 247°; 3,6-bis(4-cyanobenzyl, 70, 250° (decomposition).

IT **7670-68-0, 2,5-Piperazinedione, 3,6-bis[imidazol-4(or 5)-ylmethylene]- 7670-69-1, 2,5-Piperazinedione, 3,6-bis(2-pyridylmethylene)-**
(preparation of)

RN 7670-68-0 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(imidazol-4-ylmethylene)- (9CI) (CA INDEX NAME)



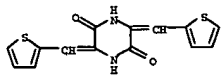
RN 7670-69-1 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1958:65835 CAPLUS
DOCUMENT NUMBER: 52:65835
ORIGINAL REFERENCE NO.: 52:11833b-c
TITLE: Synthesis of β-2-thienylalanine
AUTHOR(S): Gol'dfarb, Ya. L.; Fabrichnyi, B. P.; Shalavina, I. F.
CORPORATE SOURCE: N. D. Zelinskii Inst. Org. Chem., Moscow
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1958) 98-100
CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Heating 8.5 g. dioxopiperazine, 20.8 g. 2-thiophenecarboxaldehyde, 25 g. NaOAc, and 35 ml. Ac2O 8 hrs. at 130° gave, after aqueous treatment and leaching with hot EtOH, 15.2 g. yellow 2,5-di(2-thenylidene)-3,6-dioxopiperazine, decompose 310-14°, reduced with Na-Hg in EtOH to 2,5-di(2-thenyl)-3,6-dioxopiperazine, decompose 263-5° (EtOH), which, hydrolyzed with aqueous Ba(OH)2 24 hrs. gave 57% 2-C4H3SCH2CH(NH2)CO2H, decompose 268° (H2O).

IT **105975-15-3**, 2,5-Piperazinedione, 3,6-di-2-thenylidene-
(preparation of)

RN 105975-15-3 CAPLUS
CN 2,5-Piperazinedione, 3,6-bis(2-thienylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1942:39210 CAPLUS
DOCUMENT NUMBER: 36:39210
ORIGINAL REFERENCE NO.: 36:6159d-i
TITLE: Synthesis of the three isomeric dl- β-pyridylalanines
AUTHOR(S): Niemann, Carl; Lewis, Richard N.; Hays, John T.
SOURCE: Journal of the American Chemical Society (1942), 64, 1670-82

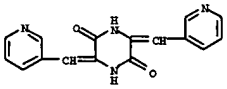
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 36:39210

AB dl-β-(2-Pyridyl)alanine (I), m. 205.5-6°, results in 17% yield from (2-pyridylmethyl)amine through (2-pyridylmethyl)benzamidomalonic ester, an oil, by refluxing with 49% HBr; Overhoff, Boeke and Gorter (C. A. 30, 5223.4) give 216° as the m. p. of I. Picolinic hydrazide and PhSO2Cl in C5H5N give a quant. yield of picolinic phenylsulfonylhydrazide (II), m. 202-3.5°; heating 25 g. II, 24 g. anhydrous Na2CO3 and 100 ml. C3H5(OH)3 at 160° for 2 min. gives 20% of picolinaldehyde (III); the failure of III to condense with hippuric acid or diketopiperazine (IV) is due to side reactions which lead to loss of III through tar formation. Nicotinic hydrazide gives 96% of nicotinic phenylsulfonylhydrazide, m. 186-6.5°; this gives 22.5% of nicotinaldehyde (V). V has greater resonance energy than III and more closely resembles the aromatic aldehydes than does III. Heating 0.67 g. of V, 1 g. of acetylthiohydantoin, 0.53 g. anhydrous AcONa and 5 ml. Ac2O at 110-15° for 30 min., the product extracted with hot H2O and the residue refluxed for 6 hrs. with 6 ml. Ac2O, 6 ml. HI and 1.3 g. red P give 60% of 5-(3-pyridylmethyl)thiohydantoin, m. 249-52°. V and IV with Ac2O and AcONa give 50% of dinicotinylidenediketopiperazine (VI), yellow, m. above 300°; refluxing 9.7 g. of VI with 6.7 g. red P, 67 ml. HI and 67 ml. Ac2O for 6 hrs. gives 69% of dl- β-(3-pyridyl)alanine (VII), m. 262-3°; it has a very sweet taste, gives a violet color with ninhydrin, and forms a dipicrate, m. 187-9°. Isonicotinic phenylsulfonylhydrazide, m. 193-4°, 93%; decomposition gives only traces of the aldehyde. 4-(Pyridylmethyl)amine (3.8 g.) and AgNO3 give 2.5 g. of 4-pyridylcarbinol-HCl (VIII), m. 167-72°; refluxing 1.8 g. of VIII with 15 ml. 49% HBr gives 2.8 g. of 4-pyridylmethyl bromide-HBr (IX), m. 145-50°; this has a very irritating action on the skin. IX (2.8 g.) gives 0.24 g. of a condensation product with the Na derivative of benzamidomalonic ester, m. 106-7°, hydrolysis of which yields 0.11 g. of dl-β-(4-pyridyl)alanine (X), m. 235-6°; ninhydrin gives a red color. The apparent dissociation consts. KB1 + 10-10, KB2 + 10-13 and KA + 10-10, are: I, 0.89 ± 0.05, 2 ± 1, 6 ± 1; VII, 3.7 ± 0.5, 5 ± 1, 8 ± 1; X, 6 ± 1, -, -. The effect of structure on acid and base strength is discussed.

IT **41668-18-2**, 2,5-Piperazinedione, 3,6-bis(3-pyridylmethylene)-
(preparation of)

RN 41668-18-2 CAPLUS

CN 2,5-Piperazinedione, 3,6-bis(3-pyridinylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1931:13822 CAPLUS
DOCUMENT NUMBER: 25:13822
ORIGINAL REFERENCE NO.: 25:1508c-e
TITLE: Spectrochemical study of amino acid anhydrides. IV. Light absorption of derivatives of azlactones, diketopiperazine, hydantoin and thiohydantoin
AUTHOR(S): Asahina, Tie-ichi
SOURCE: Bulletin of the Chemical Society of Japan (1930), 5, 354-65
CODEN: BCSJA8; ISSN: 0009-2673
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

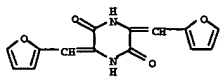
GI For diagram(s), see printed CA Issue.

AB cf. C. A. 24, 298. The ultraviolet absorption of azlactones of substituted hippuric acids, RCH:C.CO.O.CPh:N where R is o- (I), m- (II), or p-AcOC6H4 (III), o- (IV), m- (V), or p-MeOC6H4 (VI); of RCH:C(CO2H)NHCOPh, where R is furyl (VII), Ph (VIII), o-, m- or p-HOC6H4 (XV), o-, m- or p-MeOC6H4 (XVI); dibenzal- (IX), and difurfuraldiketopiperazine (X); 4-benzal- (XI), and 4-furalhydantoin (XII); 2-thiohydantoin and its following derivs.: 3-acetyl, 3-benzoyl, 3-acetyl-4-benzyl, 4-(benzyl, 4-(p-hydroxybenzyl), 4-benzal (XIII) and 4-fural (XIV). VII, X, XII and XIV are more bathochromic and hyperchromic than VIII, IX, XI and XIII. I, II and III have an absorption maximum near 3580 A. U. IV and VI have the same maximum while V is less bathochromic. The azlactones are far more bathochromic than their hydrolysis products, XV and XVI. Absorption curves and methods of preparation are given.

IT **114932-14-8**, 2,5-Piperazinedione, 3,6-difural-
(spectrum of)

RN 114932-14-8 CAPLUS

CN 2,5-Piperazinedione, 3,6-bis(2-furanylmethylene)- (9CI) (CA INDEX NAME)



L7 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

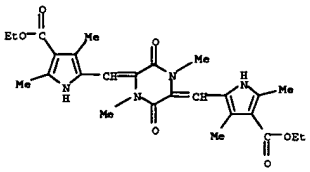
ACCESSION NUMBER: 1928:4734 CAPLUS
DOCUMENT NUMBER: 22:4734
ORIGINAL REFERENCE NO.: 22:588f-i,589a
TITLE: Some pyrrole derivatives. II
AUTHOR(S): Kuster, Wm., Koppenhofer, G.
SOURCE: Z. physiol. Chem. (1927), 172, 126-37
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Synthetic pyrrylamino acids are of interest in connection with the study of the prosthatic group of the blood pigment. The condensation of formylpyrrole derivs. with diketopiperazine, followed by hydrogenation and opening of the anhydride ring, affords a method for preparing alanine derivs. of this type. 2,2-Di(3,5-dimethyl-4-carbethoxypyrryl)-2,5-diketopiperazine (I), red crystals, m. 268-9°, was obtained in 60% yield by refluxing a mixture of 3,5-dimethyl-4-carbethoxy-2-formylpyrrole and glycine anhydride with AcOH and NaOAc. Its di-Me derivative, red crystals, m. 156°, was prepared by treating the Ag salt of I with MeI. Reduction of I in EtOH by Al-Hg and neutralization with dilute H2SO4 gave an almost quant. yield of colorless 2,2-di[3,5-dimethyl-4-carbethoxypyrrylmethyl]-2,5-diketopiperazine (II), m. 122°. Attempts to prepare a monopyrral derivative of diketopiperazine were unsuccessful, both CH2 groups of the latter being equally reactive. Hydrolysis of II by Ba(OH)2 gave 55% of β-[3,5-dimethyl-4-carbethoxypyrryl-2]-alanine (III), which decomps. 180-6° and does not form a Cu salt. Another method of preparing III consists in condensing the formylpyrrole with rhodanin, hydrolyzing the rhodanin ring, converting the resulting thioketonic acid into the oxime and reducing the latter. 3,6-Dimethyl-4-carbethoxy-2-pyrralrhodanin (IV), red needles, m. 253-5°, was obtained in 80% yield by refluxing the formylpyrrole and rhodanin with AcOH and NaOAc; phenylhydrazone, red needles, m. 272-5° (decomposition). Hydrolysis of IV by Ba(OH)2 converted it into 3,5-dimethyl-4-carbethoxy-2-pyrrylthiopyruvic acid (V), decomps. 196°; oxime, m. 210°. Reduction of the oxime by Na-Hg in the presence of lactic acid gave 62% of III. Hydrolysis of the CS group in V by heating in a sealed tube with ClCH2CO2H converted it into 3,5-dimethyl-4-carbethoxy-2-pyrrylpyruvic acid, m. 192°. 1-Phenyl-2,5-dimethyl-3-carbethoxypyrrole was condensed with aminoacetal by heating with concentrated HCl, forming di[1-phenyl-2,5-dimethyl-3-carbethoxy-4-pyrryl]-β-aminoethane, m. 246°. Similarly, 1-phenyl-2,5-dimethyl-4-carbethoxypyrrole with CH2O and HCl yielded di[1-phenyl-2,5-dimethyl-4-carbethoxy-3-pyrryl]methane, m. 102°.

IT **858834-13-6**, 2,5-Piperazinedione, 3,6-bis[(4-carboxy-3,5-dimethyl-2-pyrryl)methylene]-1,4-dimethyl-, diethyl ester **858850-88-1**, 2,5-Piperazinedione, 3,6-bis[(4-carboxy-3,5-dimethyl-2-pyrryl)methylene]-, diethyl ester
(preparation of)

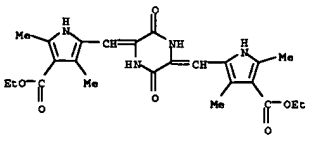
RN 858834-13-6 CAPLUS

CN 2,5-Piperazinedione, 3,6-bis[(4-carboxy-3,5-dimethyl-2-pyrryl)methylene]-1,4-dimethyl-, diethyl ester (3CI) (CA INDEX NAME)



RN 858850-88-1 CAPLUS

CN 2,5-Piperazinedione, 3,6-bis[(4-carboxy-3,5-dimethyl-2-pyrryl)methylene]-, diethyl ester (3CI) (CA INDEX NAME)



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